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A STUDY OF HYDROLYSIS BY CONDUCTIVITY METHODS.

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In aqueous solutions of the hydrochlorides of weak bases the salts are partially hydrolyzed as represented by the equation:

$$RNH_3Cl + H_2O \rightleftharpoons RNH_2OH + HCl. \qquad (1)$$

The analytical determination of the proportions of free acid, base, and salt in such solutions is a matter of importance, because from the data obtained the affinity constants of the weak bases can be calculated.[1] The most accurate method of analysis is that of Walker,[2] who determined the amount of free acid by catalysis of methyl acetate. But the most rapid method is undoubtedly the one based on conductivity measurements of the solutions, as developed by Walker, and especially by Bredig. In an investigation of the velocities of rearrangement of *o*-aminophenyl alkyl carbonates in solutions of their hydrochlorides,[3] one of us recently had occasion to require an almost instantaneous method of analyzing such solu-

[1] Arrhenius: Ztschr. phys. Chem., **5**, 17 (1890); Bredig: *Ibid.*, **13**, 213, 321 (1894).
[2] *Ibid.*, **4**, 319 (1893).
[3] Stieglitz and Upson: This JOURNAL, **31**, 458 (1904).

tions, the proportion of free acid increasing rapidly and continuously by the process of rearrangement, as expressed summarily in

$$(\text{Acyl O})\text{RNH}_2\text{Cl} \rightarrow \text{HO.R(NH Acyl)} + \text{HCl}. \quad (2)$$

The conductivity method was the only one sufficiently rapid for the purpose.

The directly observed molecular conductivity M_v of such a solution is made up of the conductivity μ_v of the non-hydrolyzed salt and the conductivity μ_{HCl} of the free acid, since the conductivity of the free weak base can be neglected as minimal in the presence of its salt. If x represents the percentage of hydrolyzed salt, then, according to Walker,

$$M_v = (1-x)\mu_v + x\mu_{HCl}, \quad (3)$$

and

$$x = \frac{M_v - \mu_v}{\mu_{HCl} - \mu_v}. \quad (4)$$

In the application of this equation various investigators have given different interpretations to the value of μ_{HCl}, the molecular conductivity of hydrochloric acid. Walker considered it to be the molecular conductivity of the acid for the original concentration of the salt solution, *i. e.*, for a completely hydrolyzed salt. Bredig, to whom we owe the most important work in the establishment of the method, used the value 383[1] as "the nearly constant molecular conductivity of the free hydrochloric acid at 25°." This is also the interpretation used in Vaubel's Physikalische Methoden der Quantitativen Bestimmung Organischer Verbindungen.[2] Winkelblech, working under Bredig, later again used Walker's interpretation.[3] Ley,[4] in an extended and important study of hydrolysis, took for μ_{HCl} the molecular conductivity of hydrochloric acid at infinite dilution, 393. Of these various interpretations, the one of Walker seemed to us the most trustworthy on the basis of the following views:

If in an n-th normal solution of a hydrochloride such as

[1] In reciprocal mercury units.
[2] P. 292 (1902).
[3] Ztschr. phys. Chem., **36**, 356 (1901).
[4] *Ibid.*, **30**, 193 (1899); also Ber. d. chem. Ges., **34**, 2626 (1901).

aniline hydrochloride, x per cent of the salt is hydrolyzed, the hydrochloric acid formed, no matter how little of it is produced, does not ionize to the same degree as it would if it were dissolved alone in all the water present. It has the chlorine ion in common with the salt. We can assume the acid as sharing the water with the salt[1] in the proportion of $x : (1-x)$, producing a mixture of x cc. n-th normal hydrochloric acid and $(1-x)$ cc. n-th normal non-hydrolyzed aniline hydrochloride. Both the acid and the salt being nearly equally ionized in equivalent solutions, they would contain the common ion in almost equal concentrations and form approximately isohydric solutions. Each would then have the molecular conductivity of the n-th normal solution.

If such is the case equation (4) would read

$$x = \frac{M_v - \mu_v}{\mu_{HCl(v)} - \mu_v}, \qquad (5)^2$$

the symbols having the same significance as in (4) excepting that $\mu_{HCl(v)}$ is always the molecular conductivity of hydrochloric acid for the original concentration of the salt solution used. If the degree of hydrolysis becomes very large, for instance 50 per cent and more, equation (5) would still hold, as we have simply mixtures containing larger proportions of the isohydric acid, of the same normality as before. If, as in the case under investigation by one of us, by a rearrangement of a salt according to (2) the free acid should accumulate more and more and finally be the sole electrolyte present—the salt disappearing in proportion as the acid is formed—equation (5) would hold continuously. If an excess of acid were added to the original solution, a similar determination of the total free acid could still be made (see below).

In the development of (5) two assumptions have been made. The first is that in equivalent dilute solutions the de-

[1] Arrhenius: Ztschr. phys. Chem., **2**, 288 (1888) and **31**, 206 (1899).

[2] Another form of the same equation is:

$$x = \frac{k_{obs.} - k_v}{k_{HCl(v)} - k_v}, \qquad (5)$$

in which the symbols stand for the respective specific conductivities. Since specific conductivities are found before the molecular, it is often more convenient to use this form of the equation.

grees of ionization of the salt and free acid may be considered to be practically the same—an assumption which is not absolutely true but which is frequently made in similar cases. For N/32 solutions of hydrochloric acid and potassium chloride the degrees of ionization are 97 and 90 per cent respectively. The second assumption is that solutions of equal concentrations of a given common ion may be considered isohydric. This has been proved to be true for weak acids which obey Ostwald's dilution law[1] and is also true as a matter of experience for strongly ionized substances such as ammonium and potassium chlorides.[2]

In view of the difference shown in the interpretation of Walker's formula, as explained above, it was thought best to test by means of mixtures of a salt and of a strong acid, of known content, its range of reliability, particularly for very strongly hydrolyzed solutions containing much acid.[3] Two series of experiments were made. The first was intended to test the application of (5) to the analysis of mixtures of hydrochloric acid and potassium chloride of varying concentrations but especially for N/32 solutions of each. In the second place equation (5) was used to ascertain the condition of equilibrium in solutions of aniline hydrochloride containing an excess of hydrochloric acid.

Potassium Chloride and Hydrochloric Acid.

The measurements were made with the Kohlrausch apparatus. The wire of the Wheatstone bridge was 1 meter long and was carefully calibrated as were all the resistances, burettes, and pipettes used. The temperature was kept constant at 25° (±0.01°) by means of a large thermostat built according to Ostwald's principles. The measurements were made largely in Kohlrausch vessels, partly in those of the Arrhenius type. The acid used was repeatedly standardized against Iceland spar[4] and against sodium carbonate. The water used had a specific conductivity of 2.0×10^{-6}. Table

[1] Arrhenius: Lehrbuch der Elektrochemie, p. 179 (1901).
[2] Arrhenius: Ztschr. phys. Chem., 31, 206 (1899).
[3] Such solutions were to be studied by this method.
[4] Chem. News, 81, 73 (1897); 87, 5 (1903). Platinum vessels were used.

I., following, gives the results of a first series of measurements with N/32 solutions. The first column gives the observed specific conductivity, the second the specific conductivity calculated according to (5) from the known composition of the mixture on the assumption that the two N/32 solutions are isohydric. The third column gives the percentage of acid used in parts of the total volume of electrolyte; column 4 gives the percentage of acid found as calculated with the aid of equation (5) or (5′). The last column gives the percentage of acid found as calculated when μ_{HCl} is made 383. If μ_{HCl} is taken as μ_∞ or 393, the values found would be still lower than the ones given in this column:

Table I.

$10^6 \times k_{obs.}$	$10^6 \times k_{calc.}$	Per cent acid used.	Per cent acid found. (Equation 5′.)	Per cent acid found. ($\mu = 383$.)
3978		0.00	0.00	0.00
4625	4670	8.92	8.34	8.10
5274	5322	17.33	16.71	16.22
5711	5766	23.00	22.34	21.68
6156	6227	29.00	28.08	27.26
6535	6590	33.68	32.96	32.00
6852	6902	37.69	37.05	35.95
7116	7185	41.34	40.45	39.26
7384	7432	44.51	43.91	42.63
7613	7662	47.50	46.86	45.51
7794	7846	49.88	49.19	47.75
7798	7866	50.14	49.25	47.81
8011	8061	52.64	51.95	50.43
8240	8290	55.56	54.94	53.34
8494	8544	58.84	58.23	56.53
8740	8812	62.32	61.38	59.60
9100	9145	66.62	66.05	64.10
9472	9518	71.42	70.83	68.74
9900	9946	76.96	76.33	74.10
10418	10453	83.46	83.01	80.60
11047	10959	90.03	91.15	88.46
11735		100.00	100.00	97.00

In a second series the solutions used were weighed instead of being measured:

Table II.

$10^6 \times k_{obs.}$	$10^6 \times k_{calc.}$	Per cent acid used.	Per cent acid found. (Equation 5'.)	Per cent acid found. ($\mu = 383.$)
3995		0.00	0.00	0.00
4067	4087	1.19	0.93	0.90
4434	4480	6.27	5.66	5.50
4918	4944	12.33	11.97	11.71
5259	5311	16.97	16.30	15.85
5814	5856	24.01	23.44	22.95
6681	6723	35.18	34.64	33.68
7178	7216	41.46	40.92	40.05
8020	8048	52.25	51.91	50.48
9125	9132	66.25	66.17	64.33
10619	10603	85.20	85.44	83.07
11748		100.00	100.00	

In a last series solutions of varying normality, from N/16 to N/32, were employed. They were prepared from a solution that was N/16 in regard to the acid as well as the salt (50 cc. N/16 hydrochloric acid was mixed with 50 cc. N/16 potassium chloride solution), and that was diluted systematically in a first series with N/32 hydrochloric acid, in a second series with the corresponding solution of potassium chloride. The resulting solutions were treated as isohydric mixtures of acid and salt of an easily ascertained normality. For instance, the solution obtained by the removal of 50 cc. of the original mixture and the addition of 50 cc. N/32 potassium chloride contained 1/64 gram-molecule acid and 2/64 gram-molecule salt per liter, or a total of 3/64 gram-molecule electrolyte. It was therefore N/21.33 as regards the total electrolyte content, and a mixture of one-volume (33.3 cc.) of N/21.33 acid and two volumes (66.7 cc.) of N/21.33 salt. These equimolecular solutions being considered isohydric, the amount of free acid could be ascertained according to equation (5) by a measurement of the conductivity of the solution. The molecular conductivities of the salt and acid for these concentrations were readily found by interpolation from the values for N/16 and N/32 solutions. The latter values were determined for the solutions of acid and salt actually employed. Table III.

gives all the results: Column 1 gives the volume, in liters, containing 1 gram-molecule total electrolyte; the other columns have the same significance as in the previous tables.

Table III.

v.	$10^6 \times k_{obs.}$	Per cent acid used.	Per cent acid found. (Equation 5.)
16.0	7741	0.00	
32.0	3990	0.00	
16.0	22960	100.00	
32.0	11720	100.00	
31.75	4078	0.78	0.73
31.51	4155	1.54	1.31
31.03	4326	3.33	2.67
30.12	4692	5.88	5.61
28.44	5399	11.11	10.67
25.60	6830	20.00	19.54
21.33	9693	33.33	32.98
16.0	15374	50.00	50.16
16.0	15380	50.00	50.19
21.33	13620	66.67	67.10
25.60	12691	80.00	80.43
28.44	12241	88.89	89.50
30.12	12011	94.12	94.82
31.03	11924	96.67	98.06

Aniline Hydrochloride and Hydrochloric Acid.

With the aid of the expression developed in equation (5), a study was also made of the conditions of equilibrium in solutions of aniline hydrochloride in which the proportions of the base and acid were varied in such a way that a greater or less excess of acid was used beyond that required for salt formation. The solutions were always made of N/32 strength as regards the aniline hydrochloride, except in the last case recorded in the table, in which a N/64 solution of the salt was employed. By the use of an excess of acid they became more concentrated in regard to the total content of electrolyte and for the calculation the molecular conductivities, M_v, μ_v, and $\mu_{HCl(v)}$, were used always with reference to the volume containing 1 gram-molecule total electrolyte as explained below.

In Table IV. the first column gives the volume in liters

containing 1 gram-molecule electrolyte; in the second column the observed molecular conductivity is given. Column 3 brings the acid found in percentages of the total electrolyte present, as calculated by means of equation (5) from the observed molecular conductivities M_v and the molecular conductivities $\mu_{HCl(v)}$ of hydrochloric acid, and μ_v of the non-hydrolyzed salt for the total concentration of the electrolyte used. These conductivities were obtained by interpolation from the values for μ_{16} and μ_{32} (88.1 and 92.1) for non-hydrolyzed aniline hydrochloride,[1] and $\mu_{HCl(16)}$ and $\mu_{HCl(32)}$ (367 and 376.4) for hydrochloric acid as determined by us for the acid actually used. For instance, in the second experiment recorded in the table 1 liter of the solution contained 1/32 or 16/512 gram-molecule aniline hydrochloride and 1/512 gram-molecule excess of added acid, a total of 17/512 gram-molecule electrolyte, or 1 gram-molecule in 30.12 liters. The observed specific conductivity was 0.003702, the observed molecular conductivity, therefore:

$$M_v = 0.003702 \times 30.12 \times 1000$$
$$= 111.5$$

$\mu_{30.12}$ for aniline hydrochloride (non-hydrolyzed), is 91.8, $\mu_{HCl(30.12)}$ for hydrochloric acid is 375.4. If x represents the percentage of free acid in parts of total electrolyte, we have by substitution of these values in (5):

$$x = \frac{111.5 - 91.8}{375.4 - 91.8}$$
$$= 0.0695$$

As the excess of acid added was 1/17 or 5.88 per cent of the total electrolyte present, 1.07 per cent of acid must have been formed by hydrolysis of the aniline salt. For comparison with these results found experimentally, as just described and given in column 3, the next column brings the theoretical amount of acid in percentages of total electrolyte, which should be present according to the known affinity constant of aniline. The theoretical figures are ascertained as follows:

[1] *Vide* Bredig: Ztschr. phys. Chem., 13, 215, 322 (1894).

For the condition of equilibrium in a hydrolyzed solution of aniline hydrochloride (see equation 1), we have :[1]

$$C_s = K \times C_b \times C_a, \qquad (6)$$

in which C_s, C_b, C_a express the gram-molecules of non-hydrolyzed salt, free base, and free acid in 1 liter of the solution. K is the constant ratio[2] between the affinity constant of aniline and the degree of dissociation of water (1.2×10^{-14}), and has a known value.[3]

The application of equation (6) to the calculation of the theoretical amount of acid which should be present in our experiments will be illustrated by the calculation of the value for the second experiment in the table. As explained above in this experiment, 1 liter of the solution was made to contain 1/32 gram-molecule aniline hydrochloride and 1/512 gram-molecule excess of acid, 1 gram-molecule total electrolyte being contained in 30.12 liters, a volume which may be designated by V. The excess of acid used was 1/17 or 5.88 per cent, and if we call y the percentage of additional acid formed by hydrolysis of the salt, then the total concentration of free acid was $(0.0588 + y) : V$. The concentration of the free base was $y : V$, of the non-hydrolyzed salt $(0.9412 - y) : V$. Substituting the values in (6), we obtain :

$$30.12\ (0.9412 - y) = 40{,}000y\ (0.0588 - y).$$

Solving for y, we find y is 0.0102 and the total free acid therefore 5.88 and 1.02, or 6.90 per cent of the total electrolyte. The theoretical amount of free acid is then 6.90 per cent ; the amount found above, by means of a conductivity measurement and equation (4), was 6.95 per cent.

The last column of the table gives the excess of acid used, in percentage of the total electrolyte present.

[1] Walker : Ztschr. phys. Chem., **4**, 319 (1889).

[2] Arrhenius : *Ibid.*, **5**, 16 (1890).

[3] K was taken to be 40,000, the mean between Bredig's value (41,900) and the constant (39,000) calculated from Bredig's data by means of equation (5).

Table IV.

v.	M_v.	Per cent acid found.	Per cent acid, theory.	Excess acid, used.
31.03	105.7	4.83	4.56	3.03
30.12	111.5	6.95	6.90	5.88
28.44	124.1	11.47	11.53	11.11
28.44	124.3	11.56	11.53	11.11
25.60	147.8	20.06	20.26	20.00
21.33	183.2	33.11	33.48	33.33
16.00	227.5	49.92	50.08	50.00
16.00	227.7	50.01	50.08	50.00
21.33	278.5	66.97	66.80	66.67

The results given in Tables I. to IV. show that Walker's interpretation of μ_{HCl}, in his fundamental equation as the molecular conductivity of hydrochloric acid referred to the total electrolyte content, gives the closest approximation to the true values for the free acid, and the equation should be used in that sense in the analysis of hydrolyzed solutions by the conductivity method. Although there are more accurate methods of analysis of such solutions, this is the most rapid one and it may be used successfully in the case of solutions undergoing continuous change. An illustration of an application to the determination of the velocities of such changes and of the affinity constants of unstable weak bases will be brought in the next report on the rearrangement velocities and affinity constants of aminophenyl alkyl carbonates.

CHICAGO, January, 1904.

Contribution from the Kent Chemical Laboratory of the University of Chicago.

THE MOLECULAR REARRANGEMENT OF AMINOPHENYL ALKYL CARBONATES.[1]

BY J. STIEGLITZ AND HENRY T. UPSON.

When *o*-nitrophenyl ethyl carbonate is reduced with tin and hydrochloric acid without any special precautions, an alkali-soluble body is obtained[2] in place of the amine which aro-

[1] The experimental work described in this paper was carried out by Mr. Upson under my direction. I am glad to take this occasion to acknowledge the valuable assistance of my collaborator. He is not responsible for the theoretical treatment of the material. J. STIEGLITZ.

[2] Bender: Ber. d. chem. Ges., 19, 2268 (1886); H. N. McCoy: This JOURNAL, 21, 111 (1899).

matic nitro compounds usually give under such treatment. J. H. Ransom,[1] working under the direction of one of us, showed that the formation of the acid body, oxyphenylurethane, is due to a molecular rearrangement of the primary product of the reduction, *o*-aminophenyl ethyl carbonate. The rearrangement proceeds according to

$$H_2NC_6H_4OCO_2C_2H_5 \rightarrow C_2H_5O_2C.NH.C_6H_4OH,$$

the carbethoxyl group leaving the negative phenol group and going to the basic amino radical. Working under special conditions, Ransom was able to isolate and study both the free base itself and its hydrochloride. The free base was found to go over spontaneously, in the course of several hours, into the isomeric oxyphenylurethane; the hydrochloride, however, was found to be perfectly stable in a dry condition, but in aqueous solution it was also gradually converted into oxyphenylurethane, hydrochloric acid being liberated at the same time.

Similar migrations of acyl radicals to neighboring amine groups have been observed both before and after the investigation of Ransom, but the interesting intermediate product, the amine, was isolated only in the one case studied in this laboratory. The present work was carried out with the view to ascertaining to what extent the tendency to rearrange exists in the case of substitution-products of *o*-aminophenyl ethyl carbonate, and to what extent the amines or their salts can be isolated as intermediate products; more especially, however, it was decided to determine the velocity of the rearrangement and the factors on which the latter depends. Regarding the first two objects, it was found that all twelve of the *o*-aminophenyl carbonates investigated show the tendency to rearrangement into urethanes, and that in every single case the hydrochloride of an amine could be isolated, even when the velocity of rearrangement under ordinary conditions is an extremely high one. The results of this portion of the investigation will be found in a later paper by one of us,[2] while parts I. and II. of this paper will deal with the work on the velocity

[1] This JOURNAL, 23, 1 (1900).

[2] Upson: See a later number of this JOURNAL.

of the rearrangement of these bodies when their hydrochlorides are dissolved in water or in dilute alcohol.

PART I.

Aminophenyl alkyl carbonates may be regarded as substituted anilines; like aniline, they can be but weak bases, and it was expected that they would prove to be weaker bases than aniline—an expectation which was verified by experiment. In an aqueous solution of the hydrochloride of such a base, hydrolytic dissociation must ensue and a condition of equilibrium be established according to the well-known equation:

$$RO_2COC_6H_4NH_2Cl + H_2O \rightleftharpoons RO_2COC_6H_4NH_2OH + HCl. \quad (1)$$

Representing the concentrations of the salt, free base, and free acid by C_s, C_b, and C_a, respectively, the condition of equilibrium is expressed according to Walker[1] by the equation

$$C_s = KC_bC_a. \quad (2)$$

K is a constant and represents the ratio[2] between the affinity constant, K_b, of the base and the dissociation constant[3] of water, K_{H_2O}, so that we have

$$\frac{C_s}{C_b \cdot C_a} = \frac{K_b}{K_{H_2O}}. \quad (2')$$

The reaction according to which an aminophenyl alkyl carbonate is rearranged would be non-reversible, and it could involve both the salt (or its positive ion) and the free base, and be represented by

$$RO_2COC_6H_4NH_2Cl \rightarrow HOC_6H_4NHCO_2R + HCl, \quad (3)$$

and

$$RO_2COC_6H_4NH_2OH \rightarrow HOC_6H_4NHCO_2R + H_2O. \quad (4)$$

If only the free base in the solution were capable of rearrangement, the reaction would be expressed by (4) or by the closely related equation,

[1] Ztschr. phys. Chem., 4, 319 (1889).
[2] Arrhenius: *Ibid.*, 5, 17 (1890).
[3] 1.2×10^{-14}. Van't Hoff's "Lectures on Theoretical Chemistry," p. 133.

$$RO_2COC_6H_4NH_2 \rightarrow HOC_6H_4NHCO_2R. \quad (5)$$

It was suspected at once that the rearrangement proceeds wholly by the rearrangement of the free base (4) or (5): the stability of the dry hydrochlorides, the spontaneous rearrangement of the isolated free base, *o*-aminophenyl ethyl carbonate, and the delay in rearrangement when an excess of hydrochloric acid is added to the aqueous solution, all pointed plainly to such a conclusion. From equations (1) and (2), namely, it follows that in the presence of an excess of acid the concentration of the free base must be reduced. Now from equations (1) and (4) or (5) it would also follow that as the rearrangement reaction proceeded free hydrochloric acid would accumulate and act as a check on the further rearrangement—changing the rate of change of the total substance present, but not affecting the rate of change of the free base present, provided the rearrangement proceeds only according to equation (4) or (5).

Hydrochloric acid, which as a catalyzer is found to increase so greatly the velocity of many reactions, would then by a simple chemical action—salt formation—affect the velocity in this case negatively, and it was the idea of testing this view quantitatively that proved the greatest incentive to undertake the investigation.

At the same time it was thought desirable to ascertain whether the tendency to rearrange, as shown by the velocity constants, is augmented by an increase in the positive character of the amino group, as determined by the affinity constants of the bases examined. By such an increase the basic group might or might not exert a more powerful attraction on the neighboring negative carbethoxyl group. Finally, it was hoped to detect the effect of stereochemical influences on the reaction, if any exist.

If the two substances holding the carbethoxyl group in favorable proximity to the amine group for a migration, namely the salt and the base, rearrange with equal velocity, then for a monomolecular reaction (3) or (4) we would have

$$\frac{dx}{dt} = k(C-x), \qquad (6)$$

and $$k = \frac{1}{t}\log.\ \text{nat.}\frac{C}{C-x}, \qquad (6')$$

where k would be a constant, representing the reaction-velocity, and C the total concentration of substance, salt, and base, originally present, and x the amount changed in time t. If, on the other hand, only the free base existing in the hydrolyzed solution of the salt undergoes rearrangement, we would have

$$\frac{dx}{dt} = kC_b. \qquad (7)$$

But C_b is, in turn, according to (2), dependent on the concentration of the free acid formed by hydrolysis and liberated by the rearrangement.

The dependence of C_b on the progress of the rearrangement can be expressed as follows, according to the two simultaneous reactions, the non-reversible one of transformation,

$$RO_2CO.C_6H_4NH_2 \rightarrow HOC_6H_4NHCO_2R, \qquad (5)$$

and the reversible hydrolytic reaction,

$$RO_2COC_6H_4NH_2Cl + H_2O \rightleftarrows RO_2COC_6H_4NH_2OH + HCl. \qquad (1)$$

The total concentration of the substance used may be called 1 gram-molecule in a definite volume V (*e. g.*, 32 liters). We will let y represent the concentration of the free base at any time, t, in terms of parts of the gram-molecule in the volume V, and x represent, in the same terms, the parts of the gram-molecule rearranged to the urethane in time t. Then the concentration of the salt at the moment, t, is equal to $1-(x+y)$ gram-molecules in V liters as the total organic matter is present either as salt, base or urethane; and finally $(x+y)$ represents the concentration of the free acid at any moment, t, in gram-molecules in V liters. Equation (2) becomes then:

$$\frac{1-(x+y)}{V} = K\frac{(x+y)y}{V^2},$$

or
$$\frac{1-(x+y)}{(x+y)y} = \frac{K}{V}. \quad (8)$$

For a given constant volume (*e. g.*, V = 32), we have

$$(K : V) = K_1,$$

and
$$\frac{1-(x+y)}{(x+y)y} = K_1. \quad (8)'$$

Solving for y, we have

$$y = \frac{-(K_1x+1)+\sqrt{(K_1x+1)^2-4K_1(x-1)}}{2K_1}; \quad (9)$$

$\frac{y}{v}$ is the C_b and $\frac{x}{v}$ the x of equation (7) and substituting these values in (7), we have

$$\frac{d\frac{x}{v}}{dt} = k\frac{y}{v} \quad \text{or} \quad \frac{dx}{dt} = ky. \quad (10)$$

Introducing the value found for y in (9), we obtain from (10):

$$kt = 2K_1\int \frac{dx}{-(K_1x+1)+\sqrt{(K_1x+1)^2-4K_1(x-1)}}, \quad (11)$$

or
$$kt = \int\frac{dx}{y}.$$

If we call y_t the concentration of the base in parts of a gram-molecule in V liters, as determined according to (9) at the time t, and y_0 its concentration when $t = 0$ and $x = 0$, we have by integrating (11):[1]

$$kt = \frac{-K_1}{1+K_1y_t} + K_1 \text{ log. nat. } \left(K_1+\frac{1}{y_t}\right) - \text{log. nat. } y_t$$
$$+\left[\frac{K_1}{1+K_1y_0} - K_1 \text{ log. nat. } \left(K_1+\frac{1}{y_0}\right) + \text{log. nat. } y_0\right]. \quad (12)$$

The equations (12) and (6′) show, therefore, how the speed of the reaction would be affected by the question whether the

[1] We are indebted to Professor F. R. Moulton for this integration, and take this opportunity to thank him again for his valuable assistance.

substance undergoing rearrangement is simply the free base present by hydrolysis, or the free base and salt indifferently, and would enable us to decide this question if the necessary analytical data could be obtained.

In order to answer the question experimentally it was necessary, therefore, to determine, on the one hand, the affinity constant of equation (8), and, on the other hand, to ascertain, for any moment, the concentration of the free base (y_t) and the amount of rearrangement (x), as used in equations (9) and (12).

It may be stated at once that for the aminophenyl carbonates examined quantitatively, equation (12) was found to give the correct course of the reaction; perfectly satisfactory velocity constants are obtained from the experimental data by this equation (12), while the application of the ordinary formula for monomolecular reactions, (6), led to no constants. We have, therefore, a monomolecular rearrangement of the free base formed by hydrolysis, proceeding all the time according to the monomolecular equation at a rate of change proportionate to the free base present at any moment; simultaneously the free acid accumulating by the rearrangement suppresses the free base and retards the apparent rate of change, but it does not affect the real rate of change as referred to the concentration of the base. The experimental study of the two simultaneous reactions was a matter of considerable difficulty, but also of great interest. The methods used will now be described.

Determination of the Affinity Constants.

Of the various methods[1] for determining the affinity constants of bases, K, as used in (8), all but one were impossible of application, owing to the very rapid change in the condition of equilibrium between the base, salt, and acid, produced by the rapid rate of rearrangement. For instance, the very accurate method of determining the amount of free acid in a

[1] Warder: This JOURNAL, **3**, 340 (1882); Ostwald: J. prakt. Chem., **35**, 112 (1887); Will: Ber. d. chem. Ges., **21**, 2777 (1888); Reicher: Ann. Chem. (Liebig), **228**, 257 (1885); Walker: Ztschr. phys. Chem., **4**, 319 (1889); Bredig: *Ibid.*, **13**, 288 (1894); Loewenherz: *Ibid.*, **25**, 385 (1898); Farmer: J. Chem. Soc. (London), **79**, 863 (1901).

hydrolyzed solution of the salt of a weak base and a strong acid by catalytic decomposition of methyl acetate[1] could obviously not be applied in this case. A method allowing of nearly instantaneous results was necessary, and such a method is the conductivity method of Walker[2] and Bredig[3]. It promised the most feasible process of analysis and was therefore employed. In a solution in which a condition of equilibrium exists between a strong acid and a weak base, their salt and water, according to (1), the conductivity for a given temperature depends wholly on the amounts and concentrations of the salt and the free strong acid present.[4]

If we call the total concentration 1 gram-molecule in V liters, and the amount of free acid present p gram-molecules in V liters, then the concentration of the base is also p gram-molecules and that of the salt $(1-p)$ gram-molecules in V liters. According to the formula established in the preceding paper[5] we have then:

$$M_v = (1-p)\mu_v + p\mu_{HCl(v)}, \qquad (13)$$

where M_v represents the observed molecular conductivity and μ_v the molecular conductivity of the non-hydrolyzed salt and $\mu_{HCl(v)}$ the molecular conductivity of the free hydrochloric acid, all at the same volume V (see the previous paper). Then

$$p = \frac{M_v - \mu_v}{\mu_{HCl(v)} - \mu_v}, \qquad (14)$$

and according to (2'):

$$\frac{V(1-p)}{p^2} = K = \frac{K_s}{K_{H_2O}}. \qquad (15)$$

In order to apply equation (14) it was necessary to determine the molecular conductivity, μ_v, of the non-hydrolyzed salt at the temperature used. Bredig's method of determining μ_v directly by suppressing the free acid by means of an

[1] Walker: *Loc. cit.*
[2] Ztschr. phys. Chem., 4, 333 (1889).
[3] *Loc. cit.*
[4] Walker: *Loc. cit.*
[5] Stieglitz and Derby: This JOURNAL, 31, 449 (1904).

excess of the free base[1] was tried, but it proved a failure partly on account of the difficult solubility of the free *o*-aminophenyl ethyl carbonate, which refused to neutralize all the free acid, and partly on account of the continuous rapid formation of free acid by the rearrangement reaction. In applying the above equation, (14), μ_v is also very generally ascertained by comparison of the base under investigation with a base, similar in composition and the number of atoms contained in the molecule, for whose hydrochloride Bredig or others have determined the molecular conductivities. The molecular conductivity of the salt under investigation is simply made equal to the molecular conductivity of the corresponding salt of the nearest similar base. Even this method was not directly applicable; the rapid rate of rearrangement made it necessary to work at 0°, and the conductivities of few salts of organic bases seem to have been determined at 0°.

The reduction of the molecular conductivities of the hydrochlorides of the nearest similar bases as determined at 25° by Bredig to 0°, by means of temperature coefficients calculated by us from the careful work of Jones[2] on the conductivity of a number of inorganic salts at 0°, gave results which were entirely incompatible with the observations. For instance, the hydrochlorides of *p*-aminophenyl ethyl and methyl carbonates, which do not rearrange, and for which M_v can be determined very accurately, gave no constants[3] on applying the general equations (14) and (15) with the help of molecular conductivities reduced to 0° from Bredig's figures for 25° for bases of analogous composition.[4] For the former base we found for K 266400 ($v = 32$); 121000 ($v = 64$); 63000 ($v = 128$); etc.

A solution of the difficulty was found and the values for the molecular conductivities of the hydrochloride of *o*-aminophenyl ethyl carbonate ascertained by a determination of the molecular conductivities of the hydrochloride of the isomeric *p*-aminophenyl ethyl carbonate and by our putting those of

[1] *Loc. cit.*, p. 214.

[2] This JOURNAL, 26, 428 (1901).

[3] All of our results indicate that the temperature coefficients for salts of complex organic bases will be found a little larger than those determined by Jones for simple inorganic salts.

[4] Bredig; Ztschr. phys. Chem., 4, 216 (1889).

the hydrochloride of the ortho base equal to these same conductivities. The hydrolyzed solution of the hydrochloride of the para base is very stable in aqueous solution and permits of very accurate determinations of the observed conductivities; and as isomers of this kind have practically identical molecular conductivities, it was sufficient to determine these for the stable isomer.

The Affinity Constant of p-Aminophenyl Ethyl Carbonate and the Molecular Conductivities of Its Hydrochloride.

–The molecular conductivities of the non-hydrolyzed hydrochloride of *p*-aminophenyl ethyl carbonate were ascertained as follows: According to equation (15) we have for the aqueous hydrolyzed solution of the salt

$$\frac{v(1-p)}{p^2} = K.$$

For a second solution containing 1 gram-molecule of the salt in v_1 liters, we have

$$\frac{v_1(1-p_1)}{p_1^2} = K,$$

and therefore

$$\frac{v(1-p)}{p^2} = \frac{v_1(1-p_1)}{p_1^2} \quad \text{and} \quad \frac{p^2}{p_1^2} = \frac{v}{v_1} \cdot \frac{1-p}{1-p_1}. \quad (16)$$

Dropping for the present $(1-p) : (1-p_1)$ as nearly equal to unity for a first approximation, and making $v = 32$ and $v_1 = 128$, we obtain

$$p_{32} = 0.5\, p_{128}. \quad (17)$$

p_{32} being put equal to $0.5\, p_{128}$, a preliminary calculation of μ_{32} and μ_{128} was made by the same method as will be used presently for the final exact calculations (see equations (19), (20), (21), and (22)), and from the found approximate values of μ_{32} and μ_{128}, p_{32} and p_{128} were ascertained as first approximations by (14) and found as follows:

$$p_{32} = 0.04 \qquad \text{and} \qquad p_{128} = 0.08.$$

Inserting these values in (16) we have more accurately:

$$\frac{p^{5}_{32}}{p^{5}_{128}} = \frac{1}{4} \times \frac{1-0.04}{1-0.08}$$
$$= \tfrac{1}{4} \times 1.04,^{1}$$

and therefore

$$p_{32} = 0.51\, p_{128}. \qquad (18)$$

μ_{32} was then finally calculated as follows: According to (14)

$$p_{32} = \frac{M_{32} - \mu_{32}}{\mu_{32(HCl)} - \mu_{32}}.$$

The observed molecular conductivity[2] M_v when v is 32 at 0°, was 51.1, and the molecular conductivity of hydrochloric acid at 0° when v is 32 is 233.6.[3] Therefore

$$p_{32} = \frac{51.1 - \mu_{32}}{233.6 - \mu_{32}}. \qquad (19)$$

In the same way

$$p_{128} = \frac{M_{128} - \mu_{128}}{\mu_{128(HCl)} - \mu_{128}}. \qquad (20)$$

The differences between molecular conductivities at these dilutions are rather small and constant values, which are used, in fact, as constants at 25°.[4]

The value of this constant at 0° for $\mu_{128} - \mu_{32}$, (Δ 128, 32), was taken as 2.7[5] as the average of all the values calculated by us from Jones' results at 0°. Introducing into (20) this

[1] For the corrected values of p_{32} and p_{128} (0.038 and 0.075), $(1-p) : (1-p_1)$ is 1.039; the value used above, 1.04, needs therefore no second correction.

[2] The method used in determining all the conductivities given in this paper was that of Kohlrausch, involving the use of a Wheatstone bridge and a telephone. The conductivities are given in reciprocal mercury units. A constant temperature of 0° was maintained by means of melting ice. The hydrochlorides of the aminophenyl alkyl carbonates are very soluble in water. Even at 0° the solution takes place almost instantly. This temperature was used because at higher temperatures the rearrangement of the bases of the ortho series is so fast that satisfactory reading with the telephone could not be made. A Kohlrausch cell was used and in measuring the velocity of rearrangements by changes in conductivities, the electrodes were frequently removed from the solution and washed with pure alcohol and ether to remove any adhering deposit of an oxyphenylurethane, the insoluble product of the rearrangement.

[3] Jones: *Loc. cit.* Exactly the same value was also found by us.

[4] *Vide* Bredig: Ztschr. phys. Chem., **4**, 198 (1889); and Ley: *Ibid.*, **30**, 234 (1899).

[5] It is also close to the value found for the constant (about 3) calculated from Bredig's Δ 128, 32 for 25° by means of the temperature correction. (*Vide* footnote.)

value as well as the found values for M_{128} and $\mu_{128(HCl)}$[1] we obtain

$$p_{128} = \frac{61.0 - (\mu_{32} + 2.7)}{239.0 - (\mu_{32} + 2.7)}, \qquad (21)$$

$$p_{128} = \frac{58.3 - \mu_{32}}{236.3 - \mu_{32}}, \qquad (21')$$

from (18), (19), and (21)

$$\frac{51.1 - \mu_{32}}{233.6 - \mu_{32}} = 0.51 \frac{58.3 - \mu_{32}}{236.3 - \mu_{32}}. \qquad (22)$$

Solving for μ_{32}, we find $\mu_{32} = 43.8$.

Then μ_{128} is 46.5. As Δ 64, 32 may be put equal to 0.5 Δ 128, 32[2] μ_{64} is 45.15. Δ 512, 128 is calculated by us as 1.7[3] as the average of all of Jones' results and Δ 256, 128 is 0.5 Δ 512, 128. We have then for μ_{256} 47.4.[4]

Using these values to determine the hydrolysis constant K for *p*-aminophenyl ethyl carbonate, according to (14) and (15), we obtain the following results:

v.	M_v.		μ_v.	$100p$.		K.	
	I.	II.		I.	II.	I.	II.
32	51.0	51.19	43.8	3.79	3.89	21400	20300
64	54.94	55.20	45.15	5.11	5.25	23200	22000
128	61.09	60.90	46.5	7.58	7.48	20600	21100
256	66.33	66.33	47.4	9.82	9.82	23900	23900

Mean, K = 22000

The agreement among the values for K is quite satisfactory, which shows that the molecular conductivities as determined are sufficiently accurate. K for aniline was found by Bredig as 41000. All of these values of K mean that in accordance with equation (2) the base under investigation has an affinity constant K times as great as the dissociation constant of water, which is 1.2×10^{-14}.

[1] Jones: *Loc. cit.*

[2] See Bredig's table for 25°. Ztschr. phys. Chem., 4, 198 (1889).

[3] It is also close to the value (2) calculated from Bredig's Δ 512, 128, (4), at 25° by means of a temperature correction.

[4] Small errors in the determination of μ_v do not affect the values of the affinity constants very much, as μ_{HCl} and M_v are very much larger than μ_v in (16).

The Affinity Constant of p-Aminophenyl Methyl Carbonate and the Molecular Conductivities of Its Hydrochloride.

The same methods were applied to the determination of the molecular conductivities of the hydrochloride of *p*-aminophenyl methyl carbonate, $NH_2C_6H_4OCO_2CH_3$, and to the determination of the affinity constant of the base. It was again found that

$$p_{32} = 0.51\ p_{128}. \qquad (23)$$

In the equation developed from this relation

$$\frac{M_{32} - \mu_{32}}{\mu_{HCl(32)} - \mu_{32}} = \frac{0.51\ [M_{128} - (\mu_{32} + 2.7)]}{\mu_{(HCl)128} - (\mu_{32} + 2.7)}, \qquad (24)$$

μ_{32} is the only unknown. Introducing the known and observed values we have

$$\frac{52.8 - \mu_{32}}{233.6 - \mu_{32}} = \frac{0.51\ [62.4 - (\mu_{32} + 2.7)]}{239.0 - (\mu_{32} + 2.7)},$$

and solving for μ_{32}, we find

$$\mu_{32} = 45.9.$$

μ_{641}, μ_{128}, and μ_{256} were determined as above for the homologous base. The results obtained are given in the following table:

v.	M_v.	μ_v.	$100p$.	K.
32	52.77	45.9	3.68	22800
64	57.33	47.25	5.33	21300
128	62.42	48.6	7.25	22600
256	67.53	49.5	9.45	25900
			Mean,	23200

The agreement in the values of K is satisfactory.

The Affinity Constants of o-Aminophenyl Alkyl Carbonates.

The molecular conductivities of the non-hydrolyzed hydrochlorides of the *p*-aminophenyl alkyl carbonates having been determined, those of the hydrochlorides of the isomeric ortho bodies, the bases under investigation, may without hesitation

be taken as equal to them at the same temperature. The hydrochlorides of the three isomeric toluidines show nearly identical molecular conductivities at 25°, and at 0° the differences would be reduced to half, or even less than half, the differences at 25°.[1] From these known values of the molecular conductivities, μ_v, of the hydrochlorides of *o*-aminophenyl alkyl carbonates, the observed molecular conductivities, M_v, and the known molecular conductivity of hydrochloric acid at 0°, the affinity constants of the bases of the ortho series may be estimated according to the equations (14) and (15).

In the observed molecular conductivities, M_v, there is, however, a small error due to the fact that in the one or two minutes required to dissolve the salt in the required volume of water and to determine the conductivity with the apparatus of Kohlrausch the molecular rearrangement releases some free hydrochloric acid (equations (1) and (4)), and increases therefore the observed molecular conductivity and the apparent degree of hydrolysis a small amount, as calculated according to (14). The values of the hydrolysis constant K will consequently be found somewhat too small. In order to eliminate this not very considerable error a first approximate estimation of the degree of hydrolysis (p) and the affinity constant, K, was made according to (14) and (15) from the first values observed at the end of from one to two minutes. With the aid of these first approximate values, the velocity of rearrangement was estimated approximately but with considerable accuracy by the same methods that will be described below for the final calculation of the velocity.

The amount of rearrangement in the carefully timed interval between the first reading and the first moment when water touched the salts (one to two minutes) was then estimated with the aid of the approximate velocity constants, and in this way the condition of the solution, when t is 0, determined with sufficient accuracy. The experimental data for the hydrochloride of *o*-aminophenyl ethyl carbonate will serve to illustrate the method.

In equation (14) the specific conductivities at the dilutions

[1] Bredig: *Loc. cit.*, p. 216.

used and at 0°, k_{obs}, k_v, $k_{v(HCl)}$, may be substituted for the molecular conductivities; as specific conductivities were found first and a great many readings were made in determining the velocities, we found it often much more convenient to use the following formula in place of equation (14) for calculating the degree of hydrolysis(p):

$$p = \frac{k_{obs} - k_v}{k_{v(HCl)} - k_v}.^{1} \qquad (25)$$

The data for the approximate calculation of the degree of hydrolysis, p, of the hydrochloride of *o*-aminophenyl ethyl carbonate and of the affinity constant of the base, (equation (15)), are given in the following table. In the first column we have the volumes containing 1 gram-molecule of the substance; in the second the observed specific conductivities at 0°; in the third the specific conductivities of the non-hydrolyzed salts at 0° as calculated from the molecular conductivities (p. 469); in the fourth column the specific conductivities of hydrochloric acid at 0° according to Jones; in the fifth column the degree of hydrolysis; and in the last column the calculated affinity constant:

Table I.

v.	$10^6 \times k_{obs}$.		$10^6\, k_{salt}$.	$10^6\, k_{acid}$.	$100\, p$.		K.	
	I.	II.			I.	II.	I.	II.
32	2488	2488	1369	7300	18.9	18.9	730	730
64	1472	....	706.3	3700	25.6	...	730	...
128	876.2	836.5	363.3	1867	34.1	31.5	725	885
256	505.1	505.4	185.1	937	42.5	42.5	810	810

Mean, $K = 775$

The agreement, under the conditions used, is satisfactory.

As was stated above, and will be shown below, the rate of rearrangement is proportional to the concentration of the base present at any moment, a constant being found according to the equations (7) and (12). The following table, II., gives the data for the preliminary estimation of this velocity

[1] k_{obs} is the observed specific conductivity of the hydrolyzed solution of the salt, k_v the specific conductivity of the non-hydrolyzed salt, $k_{v(HCl)}$ that of hydrochloric acid, all for solutions of 1 gram-molecule of the substance in v liters.

constant which will be used for correcting the values just given for the time that elapsed between the first moment of solution and the first reading of the conductivity.

The concentration used was 1 gram-molecule of the hydrochloride in 32 liters. All the concentrations in the table are given as parts (per cent) of this gram-molecule in 32 liters. Column 1 gives the time in minutes; column 2 gives the free acid, p_t, present at any moment, t; the method of analysis by means of which this amount of free acid was ascertained (by conductivity measurements) for any moment will be described in detail below. The salt, s_t, (column 3) is always equal to $(1 - p_t)$ according to equation (1), and the free base b_t (column 4) is then calculated by equation (2) by insertion of the values for C_s and C_a and K(775); x, the amount rearranged in time t, is equal to $(1 - s_t - b_t)$ or $(p_t - b_t)$, (column 5). The approximate velocity constant, k, was calculated according to

$$k(t-2) = -\frac{K_1}{1+K_1 b_t} + K_1 \text{ log. nat. } \left(K_1 + \frac{1}{b_t}\right) - \text{log. nat. } b_t$$

$$+ \left[\frac{K_1}{1+K_1 b_2} - K_1 \text{ log. nat. } \left(K_1 + \frac{1}{b_2}\right) + \text{log. nat. } b_2\right], \quad (26)$$

which is derived from equation (12) by taking the time for the first reading of the conductivity, *viz.*, two minutes after the solution was made, as the starting-point for the calculation; b_2 is the concentration of the base at that moment. The constant expression in equation (26), which is bracketed, has the value —79.435, and K_1 is K : V or 775 : 32.

Table II.

t.	$100p_t$.	$100s_t$.	$100b_t$.	$100x$.	k.
2	18.9	81.1	17.7	21.16	0.056
30	30.55	69.45	9.36	25.58	0.055
40	33.7	66.3	8.12	34.95	0.059
60	40.9	59.1	5.95	40.55	0.057
80	45.5	54.5	4.95	45.85	0.057
120	53.1	46.9	3.65	49.45	0.056
150	58.3	41.7	2.95	55.35	0.057
				Mean,	$k = 0.056$

In the following table, III., we now give the data of Table I. as corrected with the aid of the velocity constant, k, for the time that elapsed between the first moment of solution ($t = 0$) and the first readings of the conductivities. Column 1 gives the volumes containing 1 gram-molecule of the substance; columns 2 and 3 give the calculated concentration of the free acid (p_0) and free base (b_0) when t is 0; this concentration must satisfy the velocity constant ($k = 0.056$) for the small time interval (t_1) and is found by successive substitution of values smaller than the degree of hydrolysis (p) given in Table I. until k is fulfilled for the small time interval t_1 when estimated as described below on this page. Column 4 gives the affinity constant calculated from p_0 and b_0 according to equation (15). Column 5 gives the time in minutes that elapsed in each experiment before the first reading was taken; column 6 gives the free acid, p_t, present when the first reading was taken, as determined analytically by the conductivity at the moment (see below). Column 7 gives the free base, b_t, present when the first reading was taken, as calculated from the concentrations of the free acid p_t and the salt $(1 - p_t)$ according to equation (2); column 8 gives the total substance, x_t, rearranged in time t_1. It is equal to $p_t - b_t$. Column 9 gives the velocity constant as calculated for the small time interval, t_1, from the preceding data; it is found by taking the concentration of the base for the short interval to be equal to the mean of the concentration of the base when t is 0 and when t is t_1 (column 5); then according to equation (7) (p. 462).

$$\frac{x}{\mathrm{V}t_1} = k\,\frac{b_0 + b_{t_1}}{2\mathrm{V}}$$

and

$$k = \frac{2x}{t_1(b_0 + b_{t_1})}. \qquad (7')$$

It is used as a test for the correctness of the values of columns 2, 3, and 4, which together with the observed values of columns 5 and 6, determine k. A small variation in the velocity constant k has a very small effect on the value of the affinity

constant, K. Since the rearrangement is a monomolecular reaction whose velocity is dependent only on the concentration of the base, equation (7′) can be applied whether v is 32, 64, 128, or 256 liters, as in the terms in which x and b are expressed above, v is eliminated in equation (7′).

Table III.

v.	$100p_0$.	$100b_0$.	K.	t_1.	$100p_t$.	$100b_t$.	$100x$.	k.
32	18.0	18.0	810	2	18.9	16.94	1.96	0.056
32	18.0	18.0	810	2	18.9	16.94	1.96	0.056
64	24.70	24.7	790	1½	25.6	23.55	2.05	0.056
128	32.95	32.95	790	1½	34.1	31.3	2.80	0.058
128	30.65	30.65	[945]	1½	31.5	29.56	2.04	0.054
256	41.50	41.50	870	1½	42.55	39.74	2.81	0.055
256	41.30	41.30	880	1½	42.55	39.25	3.30	0.055

The mean of all the values of the affinity constant K, excepting (5) which was excluded on account of its obvious discrepancy, is $K = 825$. $K = 800$ is considered, however, the more correct, as the mean of the more reliable and concordant determinations 1 to 4, in less dilute solutions, where the rate of change is smaller, as the relative amount of free base is smaller and the observations, in consequence, more accurate.

Having determined the affinity constant of *o*-aminophenyl ethyl carbonate with reasonable accuracy, we will proceed to discuss the experimental method for following the course of rearrangement of the base in the aqueous solution of the hydrochloride and the method for calculating the velocity of rearrangement from the data obtained by observation.

The Velocity of the Rearrangement of o-Aminophenyl Ethyl Carbonate in the Aqueous Solution of the Hydrochloride, at 0°.

The experimental determination of the velocity of the rearrangement in a solution of the hydrochloride of *o*-aminophenyl ethyl carbonate is based on the following considerations: The two reactions expressed by the equations

$$RO_2CO.C_6H_4NH_2Cl + H_2O \rightleftarrows RO_2COC_6H_4NH_2OH + HCl, \quad (1)$$

$$RO_2COC_6H_4NH_2OH \rightarrow HOC_6H_4NHCO_2R + H_2O, \quad (4)$$

the one reversible and the second non-reversible, take place simultaneously in this solution. As the rearrangement proceeds according to (4) the amount of free base is diminished, and consequently to restore the disturbed condition of equilibrium of reaction (1) the reaction will proceed from left to right; more free base is formed and acid thereby liberated, but, obviously, as the acid has increased, the amount of free base reproduced will be less than the amount rearranged; and as every molecule of base reproduced by hydrolysis liberates a molecule of acid, the number of molecules of acid liberated in a given time will also be smaller than the number of molecules that have been rearranged. The increase in acid will, therefore, not be a direct measure of the number of molecules rearranged. Reaction (1) being ionic can be considered to proceed instantaneously to maintain a condition of equilibrium every moment.

The course of the reaction is marked, therefore, by a continuous increase in the amount of free hydrochloric acid and of the product of rearrangement, oxyphenylurethane, and by a continuous decrease in the amount of salt and free base present. The free base, being exceedingly weak and practically non-ionized in the presence of its hydrochloride, would have no effect on the conductivity of such a solution. The same is true for the oxyphenylurethane formed; most of it is precipitated as it is formed and it is an exceedingly weak acid, and in the presence of free hydrochloric acid it is practically non-ionized and cannot affect the conductivity of the solution.[1] The conductivity depends, therefore, at any moment, solely on the relative concentrations of the salt and the free hydrochloric acid, and as the latter is a far better conductor the conductivity will steadily increase.

[1] Saturated solutions of *o*-oxyphenylurethane and of (3)-methyl-(6)-oxyphenylurethane gave, at 25°, specific conductivities of 0.00052. The conductivity of hydrochloric acid in solutions ranging from N/32 to N/100 was not changed by the addition of an excess of either urethane.

The hydrochloric acid and the salt have an ion, Cl′, in common, and as they have practically the same degree of ionization in equivalent dilute solutions, such solutions contain the common ion in the same concentration and may be considered to be isohydric. Now if we start with a N/32 solution of the hydrochloride of *o*-aminophenyl ethyl carbonate, and have, before any rearrangement has occurred, a condition of equilibrium as expressed in equation (1) with p per cent of 1 gram-molecule of free acid in 32 liters, and consequently $(1-p)$ per cent of 1 gram-molecule of salt, we can consider the solution to consist of p cc. N/32 hydrochloric acid and $(1-p)$ cc. N/32 salt solution—the acid and salt dividing the water between them in the proportion of $p : (1-p)$.[1] The specific conductivities of the acid and salt considered separately will, therefore, be the specific conductivities for N/32 solutions and the observed specific conductivity of the solution will be :[2]

$$k_{32(obs)} = (1-p)\, k_{salt(32)} + p k_{HCl(32)}. \qquad (27)$$

Now as the rearrangement proceeds according to equation (4), we continue to have a N/32 solution of chlorine ions, and if p_t represents the per cent of 1 gram-molecule acid present, at any moment, $(1-p_t)$ would still represent the per cent of salt present, (equation 1), and consequently equation (27) holds good throughout the whole course of the reaction. From (27) we find

$$p_t = \frac{k_{obs(32)} - k_{salt(32)}}{k_{HCl(32)} - k_{salt(32)}}. \qquad (28)$$

In this equation the observed specific conductivity $k_{obs(32)}$ is determined by conductivity measurements with the Kohlrausch apparatus; the specific conductivity of the non-hydrolyzed salt $k_{salt(32)}$ was determined as shown above and found to be 0.001369 at 0°. The specific conductivity of N/32 hydrochloric acid, $k_{HCl(32)}$, at 0° was found by Jones to be 0.007300. We are thus able to determine for any moment the

[1] Arrhenius: Ztschr. phys. Chem., 2, 17 (1888); 31, 206 (1899). See also the preceding paper in this JOURNAL by Stieglitz and Derby.

[2] Stieglitz and Derby: *loc. cit.*

amount of free hydrochloric acid, p_t, present in the solution during the course of the rearrangement by means of a conductivity determination at the required time.

The concentration of the base, b_t, at any moment can be determined from that of the acid. For when the concentration of the acid is p_t per cent of 1 gram-molecule in 32 liters, the concentration of the salt, s_t, is $(1 - p_t)$ per cent, and the concentration of the base, b_t, is then determined for any moment from equation (2):

$$C_s = KC_bC_a,$$

or
$$\frac{1 - p_t}{V} = K\frac{b_t}{V} \cdot \frac{p_t}{V}, \qquad (29)$$

and
$$b_t = \frac{V}{K} \times \frac{1 - p_t}{p_t}. \qquad (29')$$

K is the affinity constant of the free base and was found to be 800 (Table III., p. 475). For the concentration of the base, b_t, at any moment we have, then,

$$b_t = \frac{32}{800} \times \frac{1 - p_t}{p_t}. \qquad (29'')$$

For the amount of substance, x_t, rearranged in time, t, we have,

$$x_t = 1 - (s'_t + b_t)$$
$$= p_t - b_t.$$

From the values thus determined we can ascertain if all the aminophenyl ethyl carbonate, whether present as salt or base, is rearranging with equal velocity, by calculating the value of the velocity constant k_x according to equation (6'):

$$k_x = \frac{1}{t} \text{ log. nat. } \frac{C}{C - x}$$
$$= \frac{1}{t} \text{ log. nat. } \frac{1}{1 - x'}. \qquad (6')$$

It is shown (see Table IV., column 8, in which common logarithms were used for this constant) that no constant value for k_T is found—consequently, the free base and salt molecules do not rearrange indifferently.

By calculating the value of the velocity constant k_B according to equation (12), we can ascertain whether only the molecules of the free base are undergoing rearrangement. Equation (12) becomes

$$k_B.t = -\frac{K_1}{1 + K_1 b_t} + K_1 \text{ log. nat. } \left(K_1 + \frac{1}{b_t}\right) - \text{log. nat. } b_t$$

$$+ \left[\frac{K_1}{1 + K_1 b_0} - K_1 \text{ log. nat. } \left(K_1 + b_0\right) + \text{log. nat. } b_0\right].$$

$$K_1 = \frac{K}{V} \text{ or } \frac{800}{32} = 25.$$

b_0, the concentration of the base when t is 0, has the value 0.1810 molecule in 32 liters (see Table III.). Introducing these values we obtain:

$$k_B.t = -\frac{1}{0.040 + b_t} + 25 \text{ log. nat.} \left(25 + \frac{1}{b_t}\right) -$$

$$\text{log. nat. } b_t - 82.664. \quad (30)$$

As is seen from the following table, where the values of k_B are given in column 7, they show a very good agreement for the long time interval between $t = 20$ and $t = 600$, when it was possible to make the conductivity readings with considerable accuracy. During the first twenty minutes when the amount of the free base was large and the conductivity changing, therefore, very rapidly, parallel with the rapid change of the base, the readings with the Kohlrausch apparatus and a telephone were necessarily much less accurate; the constant was determined, therefore, only for the time after $t = 20$. The determination leaves no doubt whatever, first, that the substance undergoing rearrangement in the solution of the hydrochloride of *o*-aminophenyl ethyl carbonate is the free base formed by hydrolysis, and that its rearrangement is a

monomolecular reaction, the velocity for which at a given temperature is dependent only on the concentration of the base, and second, that the rearrangement is influenced by the presence of the hydrochloric acid only in so far as the latter converts the free base into the salt.

The value for the velocity constant, k_B, can also be calculated from the experimental data by the following very close approximation: for small time intervals (*e. g.*, $t = 10$ minutes) the concentration of the base may be considered to be the average of its concentrations at the beginning and the end of the time interval. If b_0 represents the concentration of the base when $t = 0$, and $b_1, b_2, \ldots\ldots b_{n-1}, b_n$ express the concentrations at the end of the first, second, $(n-1)$th and nth time interval at ten minutes, then for a monomolecular reaction dependent on the concentration of the base,

$$k = \frac{x}{10\left(\frac{b_0}{2} + b_1 + \ldots\ldots b_{n-1} + \frac{b_n}{2}\right)}. \qquad (30')$$

The results for the velocity constant calculated on the basis of this formula are given in column 6 as k'_B; for the time beyond $t = 150$, interpolated values were used and a member, b, included in the summation for every ten minute interval. The results agree very well with those obtained by means of the more rigorous formula (30).

The table follows: Column 1 gives the time in minutes; 2, the observed specific conductivities; 3, the concentration of acid, p_t, in percentages of 1 molecule as calculated according to (28); 4 gives the percentage of free base, b_t, present as calculated from (29″); in column 5 the percentage of rearranged substance is given; 6 gives the velocity constant calculated according to (30′); 7 the same calculated according to (30). The last column gives the results of the calculation of a velocity constant on the basis of the ordinary equation for a monomolecular reaction involving all of the substance present (equation (6′)).

Table IV.

t.	$10^6 k_{obs.}$	$100p_t$.	$100b_t$.	$100x$.	k'_B.	k_B.	k_T.
0		18.1	18.10				
2	2489	18.9	17.14	1.76			
10	2643	21.5	14.61	6.89	[0.042]	[0.0425]	311
20	2872	25.3	11.81	13.49	[0.046]	[0.0464]	315
30	3181	30.55	9.10	21.45	[0.0535]	0.0566	349
40	3369	33.7	7.87	25.83	[0.0535]	0.0555	324
50	3640	38.2	6.47	31.73	0.0570	0.0610	331
60	3800	40.9	5.78	35.12	0.0570	0.0600	314
70	3904	42.7	5.37	37.33	0.0556	0.0571	291
80	4070	45.5	4.79	40.69	0.0563	0.0583	284
90	4190	47.5	4.42	43.08	0.0560	0.0570	272
100	4337	50.0	4.00	46.00	0.0567	0.0586	268
110	4404	51.2	3.81	47.39	0.0558	0.0567	254
120	4520	53.1	3.53	49.57	0.0560	0.0569	248
130	4642	55.2	3.25	51.95	0.0565	0.0578	245
140	4720	56.5	3.08	53.42	0.0561	0.0571	237
150	4825	58.3	2.85	55.50	0.0560	0.0581	234
180	5052	62.1	2.44	59.70	0.0562	0.0571	219
210	5301	66.3	2.03	64.30	0.0569	0.0588	213
240	5401	68.0	1.88	66.10	0.0556	0.0554	196
270	5651	72.2	1.54	70.60	0.0568	0.0591	197
300	5725	73.6	1.435	72.40	0.0562	0.0574	186
330	5881	76.1	1.256	74.80	0.0563	0.0572	181
360	6048	79.0	1.063	78.00	0.0572	0.0601	183
390	6134	80.4	0.975	79.40	0.0569	0.0592	176
420	6180	81.2	0.926	80.30	0.0565	0.0571	168
540	6410	85.1	0.700	84.40	0.0556	0.0567	149
650	6610	88.4	0.525	87.90	0.0564	0.0581	153
1500	7301	100.0	0.000	100.0			
				Means,	0.0564	0.0578	

k_B can also be calculated as follows. Equation (12) gives :

$$k(t_2-t_1) = -\frac{K_1}{1+K_1b_2} + \frac{K_1}{1+K_1b_1} + K_1 \text{ log. nat. } \frac{K_1+\frac{1}{b_2}}{K_1+\frac{1}{b_1}} + \text{log. nat. } \frac{b_1}{b_2}. \quad (31)$$

A few estimations for time intervals chosen at random follow :

Table V.

t_2.	t_1.	t_2-t_1.	k_B.
100	60	40	0.0564
150	50	100	0.0566
150	80	70	0.0578
300	100	200	0.0555
600	100	500	0.0580
		Mean,	0.0569

In a duplicate determination of the velocity of rearrangement, readings were not made as often as above. The agreement between the two series is satisfactory, as shown by the following table:

Table VI.

t.	$10^6 \times k_{obs}$.	$100p_t$.	$100b_t$.	$100x$. I.	$100x$. II.	k_B.
0		18.10	18.10			
2	2489	18.90	17.20	1.7	1.7	
30	3169	30.35	9.18	21.4	21.2	0.0556
62	3816	41.25	5.70	35.60	35.55	0.0593
77	3975	43.93	5.10	39.55	38.80	0.0557
167	4949	60.35	2.63	57.90	57.70	0.0569
390	6112	80.00	1.00	79.40	79.00	0.0581
					Mean,	0.0571

In the fifth column, under $100x$, the total rearrangement for equal times, is compared for the duplicates.

Orthoaminophenyl Methyl Carbonate.

The determinations of the affinity constant of *o*-aminophenyl methyl carbonate and of the velocity constant of its rearrangement in the aqueous solution of its hydrochloride were carried out in the same way as in the case of the ethyl ether, as just described. By putting the molecular conductivities μ_v of the non-hydrolyzed chloride equal to the corresponding conductivities of the non-hydrolyzed hydrochloride of the isomeric base, *p*-aminophenyl methyl carbonate, as determined above (p. 470), it was possible to determine the affinity constant according to Walker's and Bredig's method.

As there was some rearrangement of the hydrochloride with production of an excess of acid during the short time interval between the solution of the salt and the first readings, the values obtained by using these first readings for an approximate determination of the affinity constants were corrected with the aid of a preliminary approximate determination of the value of the velocity constant of rearrangement—in exactly the same way as described above in detail for the ethyl ether. It will only be necessary to give the experimental data in the following tables. The first shows the approximate estimation of the affinity constant K:

Table VII.

v.	M_v.		μ_v.	$100x$.		K.	
	I.	II.		I.	II.	I.	II.
32	78.5	....	45.90	17.37	....	877	...
64	94.78	93.5	47.25	25.08	24.20	761	829
128	108.16	108.16	48.60	31.30	31.30	899	899
256	125.61	125.60	49.50	39.97	39.97	960	960

Mean, K = 880

The approximate velocity constant of rearrangement, k, determined as on page 473, was found to be 0.090 as the mean of eighteen observations (from twenty-three to two hundred and twenty-nine minutes); the values ranged from 0.0875 to 0.0924, but fourteen were between 0.089 and 0.0915. The correction of the data of the previous table, with the help of this approximate velocity constant ($k = 0.090$) is given in the next table. The method of correction and the meaning of the columns are explained in connection with Table III.:

Table VIII.

v.	$100p_0$.	$100b_0$.	K.	t_1.	$100p_{t_1}$.	$100b_{t_1}$.	$100x$.	k.
32	16.10	16.10	1035	2	17.37	14.70	2.67	0.087
64	22.40	22.40	990	2	24.20	20.25	3.95	0.092
64	23.30	23.30	[905]	2	25.08	21.13	3.95	0.089
128	29.40	29.40	1045	1¾	31.30	26.90	4.40	0.089
128	29.40	29.40	1045	1¾	31.30	26.90	4.40	0.089
256	38.40	38.40	1070	1¼	40.00	35.89	4.11	0.089
256	38.40	38.40	1070	1¼	40.00	35.89	4.11	0.089

Mean (excluding the third) K = 1040

The following Table IX., gives the final data for the calculation of the velocity constant, k_B, and the results obtained.

The nature of the data of the first five columns is the same as explained above for Table IV. In column 7 appear the values of the velocity constant as calculated from the concentrations of the base, b_t, for the various time intervals, t, according to equation (12). As K_1 is K : V or 1040 : 32 (*i. e.*, 32.5), and the initial concentration of the base, b_0, is 0.1607 molecule, the equation reads for this case :

$$k_B t = -\frac{1}{0.03077 + b_t} + 32.5 \text{ log. nat. } \left(32.5 + \frac{1}{b_t}\right) - \text{log. nat. } b_t - 115.458.$$

In column 6 the velocity constant (k'_B) is given as calculated by a formula corresponding to that given in equation (30′) that can very readily be adapted to the varying time intervals used.

The table shows both by the rigorous method of calculation (k_B) and the less rigorous method (k'_B) that the reaction of rearrangement is undoubtedly a monomolecular one, dependent wholly on the concentration of the free base formed by hydrolysis. While the values vary somewhat more than in the previous case, there is no question that for over eight hours a constant rate of change of the base is shown ; at that time 90 per cent of the substance had been rearranged. It is also clear that the velocity of rearrangement is nearly twice as great as for the ethyl ether of the same series ($k = 0.0578$), a fact which accounts perhaps for the somewhat greater range of experimental error in the observations :

Table IX.

Time.	$10^5 \times k_{obs.}$	$100p_t$.	$100b_t$.	$100x$.	k'_B.	k_B.
0		16.07	16.07			
2	2454	17.40	14.60	2.80		
20	3094	28.30	7.80	20.50		[0.0959]
29	3401	33.55	6.10	27.45	[0.0968]	0.0981
39	3694	38.53	4.91	33.62	0.0993	0.1028
49	3904	42.10	4.23	37.87	0.0984	0.1018
59	4138	46.10	3.60	42.50	0.1004	0.1042
69	4348	49.68	3.12	46.56	0.1019	0.1064
89	4642	54.70	2.548	52.15	0.1015	0.1049
109	4880	58.77	2.159	56.61	0.1010	0.1032
129	5112	62.72	1.829	60.89	0.1014	0.1031
149	5286	65.68	1.608	64.07	0.1008	0.1029
169	5482	68.50	1.415	67.08	0.1009	0.1023
189	5613	71.24	1.247	69.99	0.1010	0.1026
209	5803	74.50	1.053	73.43	0.1027	0.1074
229	5881	75.81	0.982	74.83	0.1018	0.1041
270	6027	78.30	0.853	77.45	0.1002	0.0979
330	6246	82.04	0.674	81.37	0.0994	0.0966
390	6482	86.06	0.498	85.56	0.1102	0.1002
450	6556	87.35	0.445	86.90	0.0986	0.0932
510	6736	90.40	0.326	90.07	0.0995	0.0990
(1440)	7280	100.00		100.00		
				Mean,	0.1005	0.1017

Cresol Derivatives.

4-Methyl-2-aminophenyl Ethyl Carbonate,

$C_2H_5O.\overset{(1)}{C}O.C_6H_3(\overset{(4)}{C}H_3)\overset{(2)}{N}H_2$.—As just shown, the substitution of an ethyl for a methyl group in the carbalkoxyl chain of *o*-aminophenyl alkyl carbonates reduces the velocity constant of rearrangement by nearly 50 per cent. A study was also made of the influence of the substitution of a methyl group in the benzene nucleus in place of hydrogen and the influence of the position occupied by the methyl group.

For this purpose the velocity constants of rearrangement of three *o*-aminocresyl ethyl carbonates were determined, compared with each other and those of the phenyl derivatives.

The conclusions arrived at will appear below, after the experimental material has been given.

For these determinations, by the methods described above, it was above all essential to know the molecular conductivities of the non-hydrolyzed salts. Advantage was taken of the fact that one of the isomers, 4-methyl-2-aminophenyl ethyl carbonate, the derivative of paracresol, rearranges so slowly that molecular conductivities of its hydrochloride could be determined with sufficient accuracy by the method developed for the stable hydrochlorides of the *p*-aminophenyl alkyl carbonates.

If p_{32} and p_{128} represent the degree of hydrolysis of the hydrochloride of 4-methyl-2-aminophenyl ethyl carbonate in N/32 and N/128 normal concentrations, we find with the aid of relations as expressed in equations (14) to (22), inclusive, by the methods described in detail above that

$$p_{32} = 0.546\, p_{128}.^{1} \qquad (32)$$

Combining (14) and (32) we have now exactly

$$\frac{M_{32} - \mu_{32}}{\mu_{HCl(32)} - \mu_{32}} = 0.546\, \frac{M_{128} - \mu_{128}}{\mu_{HCl(128)} - \mu_{128}}. \qquad (33)$$

M_{32}, as found, was 73.47 in reciprocal mercury units and M_{128} 102.70. $\mu_{32(HCl)}$ is 233.6, $\mu_{128(HCl)}$ is 239.0. $\Delta 128.32$ is 2.7.

Inserting these values in (33) and solving for μ_{32}, we find μ_{32} is 42.6. This value, it may be added, is also in perfect agreement with the change in molecular conductivity which was to be expected from the introduction of a methyl group into the hydrochloride of aminophenyl ethyl carbonate, for which we found $\mu_{32} = 43.8$.

[1] A second correction of this relation is also in this case unnecessary, since when we use the final values for p_{32} and p_{128} as determined below, we find $p_{32} = 0.546\, p_{128}$, which is identical with (32).

From μ_{32}, the molecular conductivities for 1–32, 1–128, and 1–256 normal solutions of the salt were derived as on page 469.

The following table gives the data for the determination of the affinity constant, K, for 4-methyl-2-aminophenyl ethyl carbonate:

Table X.

v.	M_v.		μ_v.	$100x$.		K.	
	I.	II.		I.	II.	I.	II.
32	73.47	73.47	42.60	16.16	16.16	1027	1027
64	87.23	86.50	43.95	22.47	22.07	985	1025
128	102.72	101.82	45.30	29.63	29.18	1026	1065
256	122.24	122.24	46.20	39.25	39.25	1010	1010

Mean, K = 1022

The agreement in the values of K found is very satisfactory, and the results confirm the reliability of the method used for the determination of the molecular conductivities.

The velocity of the rearrangement of 4-methyl-1-aminophenyl ethyl carbonate at 0° was then determined in N/32 solution of the hydrochloride by observations of the specific conductivity of the solution at frequent intervals (column 1 of Table XI.). From the specific conductivity (column 2), the amount of free acid (column 3) present at any moment was ascertained according to equation (28).

The specific conductivity (k_{32}) of the non-hydrolyzed salt in N/32 dilution at 0° is (μ_{32}: 32000) or 0.001331 in mercury units. The specific conductivity of N/32 hydrochloric acid at 0° is 0.007300. Inserting these values in (28) we have:

$$p_t = \frac{k_{obs} - 0.001331}{0.007300 - 0.001331}.$$

The concentration of the free base, b_t, at any moment (column 4) follows from the concentrations of the free acid, p_t, and the salt ($1 - p_t$) according to equation (29′); as V is 32 and the affinity constant, K, is 1020, we have:

$$b_t = \frac{32}{1020} \cdot \frac{1 - p_t}{p_t}.$$

For the amount of rearranged substance, x_t (column 5) for any time interval we have:

$$x_t = p_t - b_t.$$

The velocity constant, k_2, (column 7) of the rearrangement was calculated according to a modified form of equation (31), *viz*:

$$k(t_2 - t_1) = -\frac{K_1}{1 + K_1 b_{t_2}} + K_1 \text{ log. nat. } \left(K_1 + \frac{1}{b_{t_2}}\right) - \text{log. nat } b_{t_2}$$

$$+ \left[\frac{K_1}{1 + K_1 b_{t_1}} - K_1 \text{ log. nat. } \left(K_1 + \frac{1}{b_{t_1}}\right) + \text{log. nat. } b_t\right].$$

Putting $t_1 = 12$, b_{t_1} is found to be 0.1578.

$$K_1 = \frac{K}{V} \text{ or } \frac{1020}{32} = 31.875$$

and

$$\frac{1}{K_1} = 0.03137.$$

Introducing these values and the calculated value of the bracketted constant expression in the above integration, we have:

$$k(t - 12) = -\frac{1}{0.03137 + b_t} +$$

$$31.875 \text{ log. nat. } \left(31.875 + \frac{1}{b_t}\right) - \text{log. nat. } b_t - 112.707.$$

Column 6 gives the velocity constant, k'_2, calculated from a formula of summation corresponding to equation (30′), and adapted to the time intervals used.[1]

The tabulated results follow:

[1] Three to five minutes' intervals were used until $t = 88$. Only the observations made in the main intervals are tabulated, in the interest of economy of space; the intermediate readings for the shorter time intervals were used, however, in estimating k'_2.

Table XI.

t.	$10^5 \times k_{obs.}$	$100p_t$.	$100b_t$.	$100x$.	k'_B.	k_B.
2	2296	16.17	16.17			
6	2296	16.17	16.17			
12	2321	16.58	15.78	0.80		
21	2419	18.23	14.07	4.16	[0.0250]	[0.0252]
31	2489	19.40	13.03	6.37	0.0208	0.0204
41	2564	20.65	12.05	8.60	0.0198	0.0196
53	2642	21.96	11.15	10.81	0.0187	0.0185
63	2726	23.37	10.29	13.08	0.0192	0.0190
73	2816	24.88	9.47	15.41	0.0198	0.0198
83	2862	25.65	9.09	16.56	0.0189	0.0188
88	2901	26.30	8.79	17.51	0.0190	0.0190
98	2961	27.30	8.35	18.95	0.0188	0.0188
108	3045	28.71	7.79	20.92	0.0193	0.0193
118	3100	29.64	7.45	22.19	0.0191	0.0190
128	3157	30.59	7.12	23.47	0.0190	0.0189
138	3216	31.59	6.79	24.80	0.0190	0.0188
148	3277	32.60	6.49	26.11	0.0189	0.0190
158	3341	33.68	6.18	27.50	0.0192	0.0192
168	3368	34.12	6.05	28.07	0.0188	0.0187
178	3435	35.25	5.76	29.49	0.0190	0.0190
198	3505	36.43	5.47	30.96	0.0186	0.0183
218	3578	37.64	5.20	32.44	0.0183	0.0178
238	3654	38.03	4.92	34.01	0.0181	0.0177
278	3817	41.66	4.39	37.27	0.0181	0.0176
318	3994	44.62	3.894	40.73	0.0183	0.0181
358	4128	46.86	3.557	43.30	0.0182	0.0180
398	4230	48.58	3.322	45.26	0.0180	0.0176
438	4381	51.10	3.002	48.10	0.0182	0.0180
498	4496	53.02	2.780	50.24	0.0179	0.0173
536	4592	54.62	2.606	52.01	0.0179	0.0174
4800	7250	100.00		100.00		
				Mean,	0.0188	0.0186

It is apparent that the rearrangement is again a monomolecular reaction dependent on the concentration of the free base and proceeding with a practically constant velocity for the nine hours that the determination included; the results therefore, confirm those obtained in the phenyl series. It is noteworthy, too, that the methyl group introduced into the ben-

zene ring in the para position, as regards the migrating carbethoxyl group, should reduce the velocity of rearrangement to about one-third the value of the rearrangement constant of *o*-aminophenyl ethyl carbonate, but it has not very materially affected the relative affinity constants of the bases (1020 and 800, respectively).

5-Methyl-2-aminophenyl Ethyl Carbonate, $C_2H_5O_{\overset{1}{C}}O.C_6H_{\overset{5}{3}}(\overset{2}{C}H_3)NH_2$.—In an aqueous solution of the hydrochloride of 5-methyl-2-aminophenyl ethyl carbonate, the free base rearranges so rapidly, again, that in estimating the affinity constant of the base from the observation of molecular conductivities, a correction must be made for the change in the solutions in the one to two minutes that elapsed before the first conductivity reading could be taken. The method used is the same as that given in tables I.-III., and it will be sufficient to give the results in tabulated form :

Table XII.—The Approximate Affinity Constant.

v.	M_v.	μ_v.[1]	$100x$.	K.
32	69.05	42.60	13.85	1438
64	77.37	43.95	17.33	1760
128	92.74	45.30	24.50	1612
			Mean,	K = 1600

The velocity of rearrangement, k, as calculated on the basis of this approximate value of the affinity constant, was found to be 0.067. The correction of the data of the previous table for the time, t, that elapsed before M_v was observed, follows :

Table XIII.[2]

v.	$100\times p_0$.	$100\times b_0$.	K.	t_1.	$100\times p_t$.	$100\times b_t$.	$100x$.	k.
32	13.05	13.05	1630	2	13.85	12.18	1.67	0.066
64	16.35	16.35	2000	2	17.33	15.24	2.09	0.066
128	23.35	23.35	1800	1¾	24.50	21.92	2.58	0.065
	Mean, K = 1800							

[1] These values for the molecular conductivities were put equal to those determined above for the isomer.

[2] See Table III. for the meaning of the columns.

For the determination of the rearrangement velocity of 5-methyl-2-aminophenyl ethyl carbonate the integral equation (12) may be applied with the following values of the known constants:

$$K_1 = \frac{K}{V} \text{ or } \frac{1800}{32} = 56.25;$$

$$\frac{1}{K_1} = 0.01778.$$

b_0, the concentration of the base when t is 0, is 0.1247.

Inserting these values in equation (12) and calculating the result for the constant bracketted expression, we obtain:

$$k_2 t = -\frac{1}{0.01778 + b_t} +$$

$$56.25 \text{ log. nat. } \left(56.25 + \frac{1}{b_t}\right) - \text{log. nat. } b_t - 229.277.$$

Equation (28) gives the concentration of the free acid, p_t, after insertion of the known and found values:

$$p_t = \frac{k_{obs} - 0.001331}{0.007300 - 0.001331}.$$

Equation (29′) gives the concentration of the free base, b_t:

$$b_t = \frac{32}{1800} \times \frac{1 - p_t}{p_t}.$$

The amount of rearranged substance, x, is:

$$x_t = p_t - p_t.$$

Table XIV. gives the tabulated results:

Table XIV.

t.	$10^3 \times k_{obs.}$	$100 \times p_t.$	$100 \times b_t.$	$100x.$	$K_B.$
0		12.47	12.47		
2	2158	13.85	11.06	2.79	
10	2353	17.12	8.61	8.51	
22	2642	21.97	6.31	15.66	
32	2788	24.45	5.49	18.96	0.074
42	2992	27.83	4.61	23.22	0.076
52	3123	30.04	4.14	25.90	0.074
62	3271	32.50	3.69	28.81	0.074
72	3401	34.68	3.35	31.33	0.074
82	3541	37.03	3.02	34.01	0.075
92	3623	38.40	2.85	35.55	0.072
102	3694	39.59	2.71	36.88	0.070
112	3816	41.64	2.49	39.15	0.072
122	3903	43.08	2.35	40.73	0.071
132	3994	44.62	2.21	42.41	0.071
142	4089	46.21	2.07	44.14	0.072
172	4294	49.63	1.81	47.82	0.070
197	4404	51.47	1.68	49.79	0.067
237	4771	57.62	1.31	56.31	0.074
287	4978	61.10	1.13	59.97	0.072
327	5096	63.09	1.04	62.05	0.069
372	5300	66.50	0.90	65.60	0.070
427	5452	69.05	0.80	68.25	0.069
482	5631	72.05	0.69	71.36	0.070
657	6026	78.67	0.48	77.19	0.069
2880	7277	100.00	0.00	100.00	....
				Mean,	0.0717

Again we find that the rearrangement proceeds with a constant velocity, when the rate of change is referred to the concentration of the free base present in the solution. The shifting of the methyl group from the para to the meta position of the benzene ring (referred to the migrating carbethoxyl group) has increased the velocity of rearrangement nearly four-fold (0.0717 as compared with 0.0186), and has made the velocity constant of the reaction even surpass that of the non-methylated lower homologue of the phenyl series (0.0717 as compared with 0.0578 of the *o*-aminophenyl ethyl carbonate).

6-Methyl-2-aminophenyl Ethyl Carbonate,

$C_2H_5O\overset{(1)}{C}O\overset{(6)}{C_6}H_3\overset{(2)}{C}H_3NH_2$.—6-Methyl-2-aminophenyl ethyl carbonate is the last base for which the affinity constant and the

velocity of rearrangement were determined quantitatively by the methods used in this investigation. The rate of rearrangement is again so great that in determining the affinity constant from the observed molecular conductivities a correction was made in the usual way for the time elapsed before the readings could be taken (one to two minutes). The tabulated results follow:

Table XV.—The Approximate Affinity Constant,

v.	M_v.		μ_v.[1]	100x.		K.	
	I.	II.		I.	II.	I.	II.
32	78.50	77.40	42.60	18.80	18.22	735	790
64	99.72	94.59	43.95	26.33	26.26	680	685
128	108.82	108.82	45.30	32.79	32.79	800	800
256	125.62	125.20	46.20	41.00	40.77	900	910
					Mean,	K = 790	

The approximate velocity constant, k, of rearrangement was found in the usual way to be 0.067. The corrected data of the previous table follow, showing the corrected affinity constant of 6-methyl-2-aminophenyl ethyl carbonate[2]:

Table XVI.

v.	100ϕ_0.	100b_0.	K.	t.	100p_t.	100b_t.	100x.	k.
32	17.75	17.75	835	2	18.80	16.54	2.26	0.066
32	17.30	17.30	880	2	18.22	16.24	1.98	0.067
64	24.90	24.90	775	2	26.23	23.10	3.23	0.067
64	24.85	34.85	780	2	26.26	23.10	3.16	0.066
128	31.30	31.30	900	1¾	32.79	29.23	3.56	0.067
128	31.30	31.30	900	1¾	32.79	29.23	3.56	0.067
256	39.78	39.78	975	1¼	41.00	37.87	3.17	0.065
256	39.50	39.50	990	1¼	40.77	37.45	3.32	0.069
	Mean,	K = 880						

The velocity constant of rearrangement of this base was determined by the same method as in the previous cases. The known constants in equation (12) have the following values:

$$K_1 = \frac{K}{V} \text{ or } \frac{880}{32} = 27.5;$$

$$\frac{1}{K_1} = 0.03636.$$

b_0, the concentration of the base when t is 0, is 0.1734. Substituting these values in (12) we have:

[1] See table X.

[2] See Table III. for the method of correction and the meaning of the columns.

$$kt = -\frac{1}{0.03636 + b_t} +$$

27.5 log. nat. $(27.5 + b_t)$ — log. nat. b_t — 93.379.

The concentration of the acid, p_t, at any moment is determined by the observed specific conductivities according to (28):

$$p_t = \frac{k_{obs} - 0.001331}{0.007300 - 0.001331}.$$

The concentration of the free base, b_t, is found according to (29'):

$$b_t = \frac{32}{880} \times \frac{1 - p_t}{p_t}.$$

The amount of rearranged substance, x_t, is:

$$x_t = p_t - b_t.$$

Table XVII.

t.	$10^5\, k_{obs.}$	$100 \times p_t$.	$100 \times b_t$.	$100x$.	k_B.
0		17.34	17.34		
2	2454	18.81	15.69		
11	2726	23.37	11.92		
20	2987	27.75	9.47	18.28	[0.072]
30	3210	31.48	7.91	23.57	0.069
40	3435	35.25	6.68	28.57	0.069
51	3654	38.93	5.70	33.23	0.069
61	3817	41.66	5.09	36.57	0.068
71	3994	44.62	4.51	40.11	0.069
81	4138	47.03	4.10	42.93	0.068
91	4241	48.76	3.82	44.94	0.066
101	4381	51.10	3.48	47.62	0.067
111	4496	53.03	3.22	49.81	0.067
121	4616	55.04	2.97	52.07	0.067
131	4718	56.74	2.77	53.97	0.067
141	4797	58.24	2.61	55.63	0.067
151	4879	59.40	2.49	56.92	0.066
161	4993	61.34	2.39	59.05	0.067
184	5127	63.59	2.08	61.51	0.065
218	5367	67.60	1.74	65.86	0.065
237	5452	69.05	1.63	67.42	0.064
317	5822	75.24	1.20	74.05	0.063
382	6026	78.68	0.98	77.70	0.061
449	6245	82.34	0.78	81.56	0.062
509	6432	85.45	0.62	84.83	0.064
517	6762	91.00	0.36	90.64	0.061
1440	7216	100.00		100.00	

Mean, K = 0.066

The values for the velocity constant, k, show a satisfactory agreement, particularly for the first four hours, when the rate of change and the concentration are most favorable for accurate determinations. The slight falling off, which is noticeable in this and in most of the other determinations, is possibly due to the fact that the oxyphenylurethane which is precipitated may carry with it small amounts of the free base and gradually weaken the solution somewhat.

Summary of Part I.

The seven aminophenyl alkyl carbonates which were examined quantitatively show the following affinity constants, K_{aff}, and velocity constants of rearrangement, k:

Table XVIII.

		K.[1]	$10^{14} \times K_{aff}$.	k.
I.	4 aminophenyl methyl carbonate	23200	27800	
II.	4 " ethyl "	22050	26500	
III.	2 " methyl "	1040	1250	0.1017
IV.	2 " ethyl "	800	960	0.0578
V.	4 methyl-2-aminophenyl ethyl carbonate	1020	1225	0.0186
VI.	5 methyl-2-aminophenyl ethyl carbonate	1800	2160	0.0717
VII.	6 methyl-2-aminophenyl ethyl carbonate	880	1050	0.0659

A consideration of the table leads to the following conclusions:

1. Whereas the *p*-aminophenyl alkyl carbonates have affinity constants of the order of that of aniline ($K = 41000$),[2] the ortho derivatives are, without exception, very much weaker bases and their affinity constants are only about one thousand times as large as the dissociation constant of water.[3] This is what was expected from the greater proximity of the negative carbonate group, (OCO_2R), to the basic group, and the result is

[1] K signifies that the affinity constant of the base is K times greater than the degree of dissociation of water, 1.2×10^{-14}. See page 460. $K_{aff} = K \times 1.2 \times 10^{-14}$.

[2] Bredig: *Loc. cit.*

[3] The affinity constant of water, $[K_{H_2O} \times C_{H_2O} = C_H \times C_{OH}]$, is 1 : 55.5 of its dissociation constant, $[C_H \times C_{OH}]$, as there are 55.5 gram-molecules of water in 1 liter. The bases have therefore affinity constants, which are only about 55,000 times as great as that of water.

in accord with the observations of Ostwald and others on the relative influence of negative groups in the ortho and para positions on the affinity constants of acids.

Of the three cresyl derivatives the base which has the methyl group in para position to the amino group (5-methyl-2-aminophenyl ethyl carbonate) was found to be decidedly stronger than the isomeric bases, in which methyl is in the meta position to the amino group. This is in agreement with Bredig's determinations of the affinity constants of the toluidines—*p*-toluidine is more than twice as strong a base as *m*-toluidine.

2. The velocity constants obtained from five independent series of determinations for the bases named, in experiments covering from ten to twelve hours each, and continued until the rearrangement into oxyphenylurethanes was practically completed,[1] fully justify the main conclusion that in the salt solutions the rearrangement depends wholly on the presence of the free base in the solution, that the free acid retards the rearrangement by salt formation, and that the actual rate of rearrangement is the result of two simultaneous reactions, one a non-reversible reaction of rearrangement of the free base, the other, a reversible reaction, which results in a condition of equilibrium between the salt, water, the free acid, and the free base.

3. The actual velocity constants are of a rather high order, inasmuch as a nearly complete rearrangement (90 per cent) would occur at 0° in from forty (2-aminophenyl methyl carbonate) to one hundred and thirty minutes (4-methyl-2-aminophenyl ethyl carbonate), if all the base could be kept free continuously in such a solution.[2] This unquestionable result is rather surprising, because Ransom and the one of us were able to isolate and examine free *o*-aminophenyl ethyl

[1] In the case of 4-methyl-2-aminophenyl ethyl carbonate, which rearranges very slowly, only 52 per cent was rearranged at the end of nine hours, when the quantitative measurements were interrupted by the fall of night. In all cases the measurements were continued the next morning, the vessel remaining in ice over night, but no attempt was made to use the results for quantitative calculations, owing to the long break in the observations.

[2] For such a hypothetical case $t = \frac{1}{k} \log. \frac{C}{C-x}$.

carbonate, and while it rearranged spontaneously, even in the absence of water, the change was far from complete even in an hour at ordinary temperature. Moreover, we have been able to show that in an anhydrous, alcohol-free, ethereal solution of *o*-aminophenyl ethyl carbonate, there is still some base present after two and one-half days. It cannot be decided at present whether this characteristic feature of the rearrangement of the base is due simply to the formation of an acid, though a weak acid substance, oxyphenylurethane, which, in an ethereal solution of the free base or dissolved in the oily base itself, may retard its rearrangement somewhat as hydrochloric acid does in an aqueous solution, or whether there is a direct influence of the solvent as such on the velocity constant. It surely cannot be due, however, to any catalytic action of the hydrochloric acid in the aqueous solution of the hydrochloride, as one might suspect, as such an action would result in a rapid increase in the value of the velocity constant, k, which, as the experimental data show, does not occur.

4. The more or less positive character of the amino group as measured by the affinity constants, K, does not seem to have any paramount influence in determining the tendency of the base to undergo rearrangement as measured by the rate of rearrangement. That is shown clearly by comparing VI with VII, V with VI or VII, and particularly III with V in Table XVIII. With practically identical affinity constants, the last two bases show velocity constants standing in the ratio 5 : 1. The velocity constant depends more on changes affecting the neighboring carbalkoxyl group itself. The base containing the carbmethoxyl group rearranges nearly twice as rapidly as the base in which a carbethoxyl group is substituted for the carbmethoxyl radical. And in the same way as a substitution of methyl for hydrogen in the para position to the amino group (5-methyl-2-aminophenyl ethyl carbonate) causes the greatest difference in the strength of the base (the affinity constant is doubled), so a substitution of methyl for hydrogen in the para position to the carbonate group (4-methyl-2-aminophenyl ethyl carbonate) in turn affects the velocity constant most decidedly—reducing it to one-third its original value.

PART II.

It was early felt that more extensive data would be desirable for determining the secondary influences which affect the rearrangement of *o*-aminophenyl alkyl carbonates, and after the main question had been decided affirmatively, that the substance undergoing rearrangement in the aqueous solutions of the salts is the free base, an extended study was made of the behavior of halogen derivatives of the bases. An unexpected difficulty was encountered in the fact that the hydrochloride of every halogen *o*-aminophenyl ethyl carbonate that was prepared proved to be insoluble in water. At first this was thought to be simply a peculiarity of the hydrochloride of 4-chloro-2-aminophenyl ethyl carbonate which was first prepared, and derivative after derivative was made with the hope of obtaining a soluble hydrochloride containing a negative group to compare with hydrochlorides containing the positive methyl group in the cresol series. The rearrangement had to be studied, therefore, in a mixture of alcohol and water (1 : 1), and we were obliged to restrict ourselves for the present to qualitative comparisons of the tendency of the halogen phenyl bases to rearrange. The comparisons are made by means of quantitative conductivity measurements, which will prove the basis for a future quantitative development of the question, as soon as the molecular conductivities, μ_v, of the non-hydrolyzed salts have been determined for the solvent used. They are necessary for distinguishing quantitatively the two factors which determine the actually observed rate of change in the solution, *viz.*, the degree of hydrolysis determining the concentration of the free base and the true velocity constant of the rearrangement of the base. The qualitative results will be given briefly in this part.

The basis for the qualitative comparisons by means of conductivity measurements is as follows:

The increase in the specific conductivity of a solution containing the hydrochloride of an *o*-aminophenyl ethyl carbonate is a measure of the increase in free hydrochloric acid, and this in turn is an approximate measure of the total rate of change; it would be absolutely so if the salt were hydrolyzed accord-

ing to equation (1), just as fast as the base is destroyed. As explained before, this is not the case; the acid is always liberated at a little slower rate than that at which the rearrangement proceeds. The difference is small, however, and particularly so when an excess of acid has already been formed by the rearrangement of 20 to 30 per cent of the salt; the error, too, is always in the same direction and of the same order for bases, whose affinity constants are of the same order. These determine according to (1) the deviation from an exact ratio between the increase of acid and rate of rearrangement—while even a very large difference in the velocity constants has a smaller effect. Now, in the case of isomeric derivatives of *o*-aminophenyl alkyl carbonates, a like substitution in position 4 or 6, both meta to the basic amino group, has nearly the same effect on the affinity constants, as shown by a comparison of the bases V and VII in Table XVIII. Isomers which differ only in having position 4 or 6 occupied may, therefore, be compared with each other by this method. A substitution in position 5 (para to the amino group) always has a much more decided effect on the affinity constant (see VI in Table XVIII.), and we excluded this series of derivatives from this part of the investigation.

For the purpose of such comparison the proportion was determined between the observed change of the specific conductivity and the total increase in such conductivity for a complete rearrangement, and the time required for such a change was ascertained. The following table shows the qualitative comparison applied to the five bases which were studied quantitatively in Part I. and shows the applicability of the method as well as its limitations:

Table XIX.

III.[1]			VII.		IV.		V.		VI.	
Per cent calc.	*t.*	Per cent obs.	*t.*	Per cent obs.	*t.*	Per cent obs.	*t.*	Per cent obs.	*t.*	Per cent obs.
25	38	33	51	33	50	31	208	36	77	32
50	109	56	150	57	165	57	550	53	230	56
75	270	77	380	78	375	79	1500	..	657	78
85	450	87	596	85	590	87	...	..	...	..

[1] The Roman numerals in this line represent the numbers and names of the bases as given in Table XVIII.

Column 1 gives the percentage of the total increase in conductivity taken as a measure of the percentage of change. The next division gives for 2-aminophenyl methyl carbonate (Base III, Table XVIII.) in the second column the time in minutes required to reach the stage specified in column 1, and in the third column the true percentage of change as determined quantitatively in Part I (see Table IV.). The same data are given for the other four bases in the subsequent divisions. It is at once apparent that measured by the time taken to reach the same degree of change (they are arranged in that order) all these bases fall into the same order, as they do according to their accurately ascertained velocity constants, with the exception of the last, 5-methyl-2-aminophenyl ethyl carbonate: in this case the para position to the amino group, position (5), is occupied and modifies so decidedly the affinity constant, that the method developed cannot be applied to it, as expiained above. The table shows, then, that reliable qualitative comparisons of the tendency to rearrange may be made by this method, if isomers are compared which differ only in having position 4 or 6 (not 5), occupied.

The following table summarizes the results obtained with the halogen derivatives, giving the time in minutes required to rearrange 25, 50, 75, and 85 per cent of the bases in N/32 solutions of their hydrochlorides at 25°, in a mixture of alcohol and water (1 : 1) :[1]

[1] The amide hydrochlorides of this series are soluble in absolute alcohol and are not as a rule precipitated by the addition of an equal volume of water. They do not, however, go into solution readily when covered with a 50 per cent alcoholic solution. It was necessary, therefore, to dissolve them first in the alcohol and then to add the water. The heat generated when alcohol and water were mixed had to be taken into account. The method of proceeding which we adopted was as follows: A weighed amount which would give 50 cc. of a N/32 solution was dissolved in 25 cc. of absolute alcohol at 25°. Twenty-five cc. water which had been cooled to just 12° were then added and the vessel shaken for one-half minute in the water of a thermostat which was kept at 25° (±0°.01). The temperature of the solution at the end of this time was exactly 25°. This nearly 50 per cent alcoholic solution was then poured into the Arrhenius cell and the conductivity taken. From two to three minutes had in general elapsed before the first reading could be made.

Table XX.

No. of base.	Base.	Time required. 25 per cent.	50 per cent.	75 per cent.	85 per cent.
IV.	2-aminophenyl ethyl carbonate	7	19	35	51
VII.	2-amino-6-methylphenyl ethyl carbonate	8	26	54	85
V.	2-amino-4-methylphenyl ethyl carbonate	28	70	140	186
VIII.	2-amino-4-chlorphenyl ethyl carbonate	8	23	40	46
IX.	2-amino-6-chlorphenyl ethyl carbonate	2	4	8	12
X.	2-amino-4-bromphenyl ethyl carbonate	7	12	40	56
XI.	2-amino-4-methyl-6-bromphenyl ethyl carbonate	4	10	17	22
XII.	2-amino-4-brom-6-methylphenyl ethyl carbonate	..	..	43	57
XIII.	2-amino-4,6-dichlorphenyl ethyl carbonate	..	..	..	7[1]
XIV.	2-amino-4-chlor-6-bromphenyl ethyl carbonate	..	..	..	8[1]

The results given in the table lead to the following conclusions:

1. The methyl group in position (4) delays the rearrangement at 25°, as it does at 0° (compare base V with IV and VII).

2. At 25° a methyl group in position (6) retards the rearrangement somewhat—at 0° it caused a small acceleration (compare base VII and IV).

3. A halogen atom in position (6) always causes a very great increase in the velocity of the rearrangement, as compared with its effect in position (4); the relative velocity is, therefore, the same for the halogen derivatives as for the methyl derivatives.

4. A methyl group in position (4) retards the rearrangement also in the case of the halogen derivatives (compare IX and XI).

[1] 100 per cent.

5. The substitution of a halogen atom for hydrogen in position (4) of the aminophenyl or cresyl alkyl carbonates has a retarding effect on the velocity constant. The bases VIII, X, and XII are undoubtedly very much weaker bases[1] than aminophenyl ethyl carbonate (IV), and in consequence of the greater degree of hydrolysis of the hydrochlorides of the former bases their solutions would contain a much larger proportion of the free base. This would result in a far more rapid rearrangement, and a complete rearrangement in far shorter time, if the velocity constants were as large as that of aminophenyl ethyl carbonate (IV). The fact, therefore, that VIII, X, and XII require about the same length of time to reach the same degree of change as aminophenyl ethyl carbonate or, in fact, even a little more time than the latter, proves that their velocity constants must be smaller and probably considerably smaller than the latter. This is the most interesting result we found in this part of our work.

In conclusion it was possible to show that the substances undergoing rearrangement in the solutions of the salts of the halogen derivatives are again the free bases; if the hydrolysis is partially suppressed by the preliminary addition of an excess of acid, the rearrangement is decidedly retarded, as shown by conductivity measurements with the hydrochloride of 4-chlor-2-aminophenyl ethyl carbonate. Whereas the experiments showed that the chloride is completely rearranged at 25° in eighty minutes in N/32 solution if there is no excess of acid added, in a N/32 solution containing an excess of 1 molecule of hydrochloric acid, complete rearrangement is effected at 25° only in two hundred and sixty minutes. It is this effect of an excess of acid which made it possible to prepare and isolate at all, the hydrochlorides of two bases, like dichlor- (XIII) and chlorbromphenyl ethyl carbonate (XIV), which, without the excess of acid, are completely rearranged in seven or eight minutes.

CHICAGO, April 23, 1903.

[1] This is not only to be expected from the effect of a halogen on the strength of bases, but it is proved by the fact that the total observed increase in conductivity is three times as large for base IV. as for the halogen derivatives mentioned.

Contribution from the Kent Chemical Laboratory of the University of Chicago.

ON THE IONIZATION CONSTANTS OF PHENOLPHTHALEIN, AND THE USE OF THIS BODY AS AN INDICATOR.

By H. N. McCoy.

The theory of indicators proposed by Ostwald[1] aims to explain the two most interesting and important phenomena observed in connection with these bodies: (1) the change of color, and (2) the great difference in sensitiveness of different indicators toward weak acids or weak bases. Quite recently Stieglitz[2] has called attention to the bearing of the chromophoric theory of the change of color of indicators, the evidence for which theory has been furnished chiefly by Bernthsen[3], and Nietzki and Burckhart[4], on Ostwald's views. It was there pointed out that although the change of color is, very probably, not the immediate consequence of the ionization of the salt of the indicator, the two (color change and ionization) are practically coincident. Indicators are always either weak acids or weak bases, and the change of color is always associated with the change of the indicator into its salt, or vice versa. Ostwald has made it appear very probable that the sensitiveness of an indicator is directly dependent upon its degree of ionization as acid or base. Stieglitz has shown that although the indicator may be a pseudo-acid, as the chromophoric theory supposes, Ostwald's theory of sensitiveness is still essentially correct. The ionization constant to be considered is then the apparent constant. This is in fact the product of the constant of the equilibrium between the pseudo- and the true acid, and the real ionization constant of the latter. Similar statements apply to basic indicators.

Accepting this theory of sensitiveness, a knowledge of the ionization constants of indicators becomes of prime importance for a scientific basis of acidimetry. Bredig[5] has also recog-

[1] Lehrbuch der allgemeinen Chemie, 1, 799 (1891); "Scientific Foundations of Analytical Chemistry," p. 118 (1895).
[2] J. Am. Chem. Soc., 25, 1112 (1903).
[3] Chem. Ztg., 1892, 1956.
[4] Ber. d. chem. Ges., 30, 175 (1897).
[5] Ztschr. Electrochem., 6, 33 (1899).

nized the advantage to be derived from a knowledge of such constants and has promised some work on methyl orange. So far as I know an account of this has not yet appeared.

The work which forms the basis of this paper was started three years ago in connection with a study of the equilibrium between the carbonates of sodium, carbon dioxide, and water.[1] In titrating sodium carbonate solutions, phenolphthalein being used as indicator, it became apparent that the amount of acid required to discharge the color of the alkaline solution depended upon the amount of the indicator used; that, in fact, a state of equilibrium existed in which the concentration of the phenolphthalein was one of the factors.

In consequence of this view, it was thought that by determining the ionization constant of phenolphthalein, as an acid, a colorimetric method might be applied to determine the degree of alkalinity of solutions of sodium bicarbonate. It was found experimentally, that the addition of the calculated quantity of pure barium hydroxide to a very dilute aqueous solution of phenolphthalein developed but a fraction of the color given by the same quantity of phenolphthalein with excess of alkali. This effect was supposed to be due chiefly to hydrolytic dissociation, and it was thought that the degree of hydrolysis could be determined by colorimetric measurements, by using for comparison phenolphthalein solutions containing an excess of alkali. As phenolphthalein is a weak acid, we should have as the dynamic equation of ionization:

$$H \times Q = K_1 \times L, \qquad (1)$$

where H and Q represent the concentrations of the hydrogen and negative ions respectively, and L that of the non-ionized substance. By combining this equation with that of the ion-product of water, $H \times OH = K_{H_2O}$ we get

$$\frac{L \times OH}{Q} = \frac{K_{H_2O}}{K_1} = K, \text{ a constant.} \qquad (2)$$

If the acid is weak, as is the case with phenolphthalein, and the base is highly ionizable, this equation becomes identical with the familiar one of Walker:[2]

[1] This JOURNAL, 29, 437 (1903).

[2] Ztschr. phys. Chem., 4, 324 (1889).

$$\frac{\text{acid} \times \text{base}}{\text{salt}} = \text{a constant.}$$

The method tried consisted in adding N/200 barium hydroxide in known amounts, to 100 cc. of a N/12,000 phenolphthalein solution, which was made by dissolving chemically pure phenolphthalein in pure, freshly boiled water contained in a platinum dish. The concentration of salt formed was determined colorimetrically. The comparison solution was made by adding the requisite volume of N/12,000 phenolphthalein and one cc. of normal sodium hydroxide to sufficient water to make 100 cc. The solutions were compared in 100 cc. Nessler cylinders. Owing to the great excess of alkali in the comparison solution, the hydrolysis was so slight (see p. 512) that the total concentration of the phenolphthalein could be considered equal to that of the salt in the other solution of the same intensity of color. Table I. gives the results obtained. In each experiment 100 cc. of N/12,000 phenolphthalein were used. Column 1 gives the volume of N/200 barium hydroxide added. The ratio of total alkali to total phenolphthalein was varied from 1 : 1, first experiment, to 4 : 1, last experiment. The second column gives the volume of N/12,000 phenolphthalein required for the comparison solution. It also expresses the percentage of phenolphthalein converted into salt by the barium hydroxide. The last column gives the value of the hydrolysis constant, K, as calculated by means of equation (2). Since the ionization of a salt is almost complete in these very dilute solutions, Q, the concentration of the negative ions, may be considered practically equal to that of the red salt. L, is equal to the total concentration of the indicator minus Q, and OH to the total concentration of barium hydroxide minus Q.

Table I.

$Ba(OH)_2$. cc.	Phenolphthalein. cc.	10^6K.
1.7	8	8.8
3.4	35	2.6
5.1	54	1.7
6.8	80	0.7

These results were so far from satisfactory that the work was discontinued at that time.

The variability of K is to be ascribed chiefly to two causes: First, the presence of impurities in the distilled water, the most important being carbon dioxide; and, second, the fact that the indicator contains two phenol groups. The latter as well as the former would, by union with the alkali added, reduce the available base concentration. To avoid these difficulties a method was employed which readily gave a known hydroxyl concentration, irrespective of the presence of small amounts of acid impurities in the water, and of the phenol groups. This was done by using a rather large amount of a weak base, ammonia, in the presence of a known amount of one of its salts. An example will illustrate the idea. Suppose 2 cc. of N/10 ammonia, 10 cc. of N/10 ammonium chloride, and 0.05 cc. of N/10 phenolphthalein be added to sufficient water to give 100 cc. The concentration of the base employed would be 2000×10^{-6}, that of the indicator 50×10^{-6}, and that of the carbon dioxide present in the water[1] about 10^{-5}. If the phenolphthalein neutralizes one *extra* equivalent of base, on account of the phenol groups, and if the carbon dioxide is also neutralized, the amount of ammonia is not appreciably diminished. The hydroxyl concentration is readily calculated from the equation $NH_4 \times OH = 23 \times 10^{-6} \times NH_4OH$.[2] If neither phenolphthalein nor carbon dioxide is present, $OH = 4.6 \times 10^{-6}$, while in the above case $OH = 4.5 \times 10^{-6}$. This small difference may be neglected. Owing to the fact that the acid and acid groups are weak, the degree of hydrolysis would be great, so that the actual amount of base neutralized in this way would be much less than the above estimate. The hydroxyl concentration is also somewhat diminished in other ways. By taking these into account a more accurate value of the hydroxyl concentration may be found. Let the total concentrations of ammonium hydroxide and ammonium chloride used be represented by B and S, respectively, and call the

[1] McCoy: This JOURNAL, 29, 457 (1903).
[2] Bredig: Ztschr. phys. Chem., 13, 284 (1894).

concentration of the red salt formed, Q. For the state of equilibrium the concentration of the molecular ammonium hydroxide is less than B by the amount converted into the red salt, Q, plus the amount existing as ammonium and hydroxyl ions, and, of course, equivalent to the latter in concentration. Therefore, $NH_4OH = B - (Q + OH)$. The ammonium ions come chiefly from the ammonium chloride, but the concentration is increased by the amount of red salt, Q, plus the amount of the ionized ammonium hydroxide, OH. Therefore

$$NH_4 = S + Q + OH,$$

and since

$$OH = \frac{23 \times 10^{-6} \times NH_4OH}{NH_4},$$

$$OH = \frac{23 \times 10^{-6}(B - Q - OH)}{S + Q + OH}. \qquad (3)$$

In deducing this equation it has been assumed that the salts are completely ionized, and that the effect on the hydroxyl concentration of phenol groups and of impurities in the water may be neglected. The hydrolysis constant of phenolphthalein may then be calculated, as in Table I., by means of the equation:

$$L \times OH = K \times Q, \qquad (2)$$

by substituting for the factor OH, the value as calculated above.

The first step toward the testing of these deductions was the preparation of pure phenolphthalein. Commercial phenolphthalein is quite impure. It was readily freed from all impurities as follows: The yellow powder was treated with 1.5 volumes of cold methyl alcohol and allowed to stand several hours. It was then filtered and washed with cold methyl alcohol. This removed a large part of the yellow resinous matter. The light colored residue was dissolved in boiling methyl alcohol and the solution evaporated until it was of 25 to 30 per cent strength. Upon adding a crystal of phenolphthalein, cooling, and shaking, white crystals of the pure substance were obtained. The yield was very good.

The preparation of a solution of phenolphthalein presented some difficulties. Menschutkin,[1] and also Jones and Allen,[2] have observed that dilute ammonia in small quantity does not color an alcoholic solution of phenolphthalein. Schmatolla[3] has found that an alcoholic solution of phenolphthalein,[4] colored pale-red by a small amount of sodium hydroxide becomes intensely red upon the addition of much pure water. I have also observed that a very dilute aqueous solution, containing equivalent amounts of barium hydroxide and the indicator, is perceptibly bleached by the addition of even small quantities of alcohol. This effect was shown to be due to pure alcohol, free from all traces of acid. Some pure absolute alcohol (Kahlbaum) was rendered slightly alkaline by the addition of a few drops of a solution of barium hydroxide and then distilled, using a 15-inch fractionating-tube. Two cc. of the middle portion of the distillate were added to 100 cc. of a N/20,000 phenolphthalein solution containing an equivalent amount of barium hydroxide. The color of the solution was reduced to about half its original intensity; 0.4 cc. of alcohol added to another 100 cc. portion bleached it quite perceptibly, while 0.1 cc. of alcohol produced a scarcely noticeable effect on the color of a third portion.[5] From these results it was evident that appreciable quantities of alcohol could not be used in making up the phenolphthalein solutions to be studied.

A decinormal phenolphthalein solution was made by dissolving 3.18 grams of the substance (0.01 mol.) in sufficient pure alcohol (freshly distilled from barium hydroxide) to give a volume of 100 cc. 0.05 cc. of this solution added to 100

[1] Ber. d. chem. Ges., 16, 315 (1883).

[2] This JOURNAL, 18, 377 (1896).

[3] Ber. d. chem. Ges., 35, 3905 (1902).

[4] Waddel: J. Phys. Chem., 2, 176 (1898).

[5] The theory of Jones and Allen that a smaller degree of ionization in alcoholic solutions produces the observed effects, can (even supposing the ionization theory of indicators to be correct) scarcely apply to such dilute alcoholic solutions as I have used. The cause of the bleaching might possibly be ascribed to the possession of very weak acid properties by the alcohol. But Kullgren (Ztschr. phys. Chem., 37, 614 (1901)) has determined the velocity of saponification of methyl acetate in the presence of an excess of alcohol and found evidence that alcohol has not even faint acid properties. The cause of the action of alcohol, is, therefore, still an open question.

cc. of water gave a N/20,000 solution.[1] The standard ammonium hydroxide was prepared from a solution freshly distilled from a little barium hydroxide, in order to remove the carbonate.

The experimental process consisted in adding to about 80 cc. of pure water, contained in a Nessler cylinder, successively ammonia, phenolphthalein, and ammonium chloride, each in decinormal solution. Sufficient water was then added to give a total of 100 cc. The cylinder was stoppered, to avoid absorption of carbon dioxide, and the contents completely mixed. The comparison solution was made and used as previously described (p. 505).

In Tables II., III., IV., and V. are given the results obtained with solutions N/20,000 with respect to phenolphthalein. The fourth column gives the volume of N/20,000 phenolphthalein which, when mixed with 1 cc. of normal sodium hydroxide and sufficient water to make 100 cc., was necessary to match the color of the solution being studied. It gives also the percentage of the indicator which is converted into the red salt, in the corresponding ammoniacal solution. The fifth column gives the hydroxyl concentration as calculated by means of equation (3). The last column gives the value of the hydrolysis constant.

Table II.

	N/10 NH_4OH. cc.	N/10 NH_4Cl. cc.	N/20,000 Phenolphthalein. cc.	10^6 OH.	10^4 K.
1	2	1	36.0	42.0	0.8
2	2	2	20.0	22.0	0.9
3	2	10	3.2	4.6	1.4
4	2	20	1.4	2.3	1.6
5	2	40	0.6	1.2	2.0
				Average,	1.34

Solution 5 was rendered colorless by the addition of 0.4 cc. of N/10 hydrochloric acid.

[1] In measuring the small volumes of the solutions Meineke burettes (Centrbl., 1892, II., 193) were used. The small tube, having a total capacity of 2 cc., was graduated in hundredths of a cubic centimeter, so that it was possible to measure with fair accuracy to within 0.001 cc.

Table III.

	N/10 NH_4OH. cc.	N/10 NH_4Cl. cc.	N/20,000 Phenolphthalein. cc.	10^6 OH.	10^4 K.
1	1	0.5	30.0	39.0	0.9
2	1	1.0	15.0	21.7	1.2
3	1	5.0	2.5	4.6	1.7
4	1	10.0	0.9	2.3	2.3
5	1	20.00	Colorless	1.2	..
				Average,	1.53

Table IV.

	N/10 NH_4OH. cc.	N/10 NH_4Cl. cc.	N/20,000 Phenolphthalein. cc.	10^6 OH.	10^4 K.
1	0.5	0.2	30.0	40.0	0.9
2	0.5	0.5	15.0	20.0	1.0
3	0.5	1.0	8.0	9.8	1.0
4	0.5	2.0	3.3	5.7	1.6
5	0.5	5.0	0.8	2.3	2.8
6	0.5	10.0	Colorless	1.2	..
				Average,	1.46

Table V.

	N/10 NH_4OH. cc.	N/10 NH_4Cl. cc.	N/20,000 Phenolphthalein. cc.	10^6 OH.	10^4 K.
1	0.3	0.1	24.0	38.0	1.2
2	0.3	0.3	11.0	19.5	1.6
3	0.3	0.4	10.0	15.3	1.4
4	0.3	1.0	3.8	6.7	1.9
5	0.3	3.0	0.8	2.3	2.8
6	0.3	6.0	Colorless	1.2	..
				Average,	1.78

The average of all experiments of Tables II. to V. is $K = 1.53 \times 10^{-4}$.

The very slight solubility of phenolphthalein in pure water limited the study of the hydrolysis of its salts to extremely dilute solutions. So far as I am aware, the solubility of phenolphthalein has not been accurately determined. Approximate determinations were made by two methods. In the first 0.0318 gram (0.0001 mol.) was boiled with water. Twelve hundred cc. were required to dissolve this amount. The solution on cooling did not form a deposit. This solu-

tion was N/12,000. The second method consisted in adding to 100 cc. of N/500 ammonia known volumes of alcoholic N/10 phenolphthalein. The resulting clear solutions were each neutralized by the addition of 2 cc. of N/10 hydrochloric acid. With 0.5 cc. N/10 phenolphthalein a white precipitate formed when the solution was neutralized. With 0.3 cc. the solution was turbid, with 0.2 cc. the solution was faintly turbid, while with 0.1 cc. the solution remained clear upon neutralization, but formed a slight precipitate on standing over night. The last solution, which was evidently slightly supersaturated, was N/10,000. This concentration therefore represents the maximum that may be employed in volumetric work.

In Table VI. are given the results of a series of experiments with solutions containing N/10,000 phenolphthalein. The number of cubic centimeters of N/20,000 phenolphthalein required to make the comparison solution (fourth column) is now equal to twice the percentage of red salt formed.

Table VI.

	N/10 NH_4OH. cc.	N/10 NH_4Cl. cc.	N/20,000 Phenolphthalein. cc.	10^3 OH.	10^4 K.
1	0.5	0.5	35.0	19.8	0.94
2	0.5	0.5	30.0	20.0	1.13
3	0.5	2.0	6.0	5.6	1.81
4	0.5	2.0	7.0	5.6	1.55
5	0.5	5.0	1.7	2.3	2.7
6	0.5	5.0	1.6	2.3	2.9
7	2.0	2.0	50.0	22.0	0.66
8	2.0	10.0	9.0	4.6	0.98
				Average,	1.58

From the first series of experiments, $K = 1.53 \times 10^{-4}$; from the second series, $K = 1.58 \times 10^{-4}$. The mean is 1.55×10^{-4}, or roundly 1.6×10^{-4}. The ionization constant of phenolphthalein, considered as an acid, being called K_1, we have

$$K_1 = \frac{K_{H_2O}}{K}.$$

The ion product of water[1], $K_{H_2O} = 1.2 \times 10^{-14}$. Therefore,

[1] Van 't Hoff: "Vorlesungen über theoretische und physikalische Chemie," I, 124 (1901).

$K_1 = 7.5 \times 10^{-11}$. The degree of hydrolysis of the red salt in N/100 sodium hydroxide (the concentration used in the comparison solutions) may be calculated from these figures:

$$L \times OH = 1.6 \times 10^{-4} Q;$$

$$OH = 10^{-2}.$$

Therefore $L = 1.6 \times 10^{-2} Q$; or the hydrolysis equals 1.6 per cent. This small amount may be neglected.

The Use of Phenolphthalein as an Indicator.—The chief value to be derived from a knowledge of the ionization constant of an indicator lies in the fact that it is easy to calculate, by means of this constant, the degree of accuracy with which it is possible to titrate any acid or base of known ionization constant. This may be done by considering the end-point of the reaction from the standpoint of chemical equilibrium.

The minimum concentration of the red salt of the indicator required to give to 100 cc. of alkaline water a barely perceptible color was determined. It was found that 0.4 cc. of an N/20,000 phenolphthalein solution gave to 100 cc. of N/100 sodium hydroxide a barely visible color. This solution was 2×10^{-7} normal with respect to phenolphthalein. An alkaline solution containing less than this concentration of the indicator could not be distinguished from pure water. The minimum hydroxyl concentration detectable by means of N/20,000 indicator may be calculated from the equation

$$\text{acid} \times \text{base} = K \times \text{salt}.$$

Acid $= 5 \times 10^{-5}$. Salt $= 2 \times 10^{-7}$. The average value of $K = 1.6 \times 10^{-4}$; but as the values found for solutions which were very nearly neutral were, for some reason not apparent, somewhat greater than the average, it is perhaps better to take as the value of this constant the mean of the last values found in each series of experiments, as more nearly representing the conditions existing in actual titrations. This is $K = 2.5 \times 10^{-4}$. Therefore

$$OH = \frac{2.5 \times 10^{-4} \times 2 \times 10^{-7}}{5 \times 10^{-5}} = 10^{-6}.$$

This is very near the mean value of OH in the last experiments of Tables II. to V., for solutions which were barely colorless. It follows from this, that in titrating acids, in order that the end-point may be just colorless, the hydroxyl concentration must be 10^{-6}. Since $H \times OH = 1.2 \times 10^{-14}$, H must equal 1.2×10^{-8}. That is, for a barely colorless solution OH must equal 80 H. If OH is greater than 80 H the solution will be perceptibly red.

By means of the data just obtained the minimum error involved in the titration of a weak acid, HA, of ionization constant, k_a, may be calculated. In such a case

$$H \times A = k_a HA$$
$$\frac{H}{k_a} = \frac{HA}{A}.$$

Now, for the neutralized solution (that is, at the end of the titration) A is practically equal to the total concentration of the salt, since ionization in the dilute solution will be nearly complete. The concentration of the acid not neutralized is equal to $H + HA$; but $H = 1.2 \times 10^{-8}$, and is therefore so small as to be negligible. HA/A is practically the fraction of the original acid not neutralized. It is therefore the error, E_a, of the analysis

$$E_a = \frac{H}{k_a} = \frac{1.2 \times 10_{-8}}{k_a}.$$
$$k_a = 1.2 \times 10_{-8}/E_a. \qquad (4)$$

By means of the last equation one may calculate the ionization constant of an acid which may be titrated with a given error of analysis. (It is here assumed that the volume is about 100 cc. at the end of the titration and that the concentration of the phenolphthalein is N/20,000.) If E_a is 0.1 per cent, k_a is equal to 1.2×10^{-5}. For $E_a = 0.2$ per cent $k_a = 0.6 \times 10^{-5}$. Ostwald[1] has determined the ionization constants of a large number of organic acids. In the list of over 200 acids only eight have an ionization constant less than 1.2×10^{-5}, and for four of these the value is greater than

[1] Ztschr. phys. Chem., 3, 418 (1889).

0.6×10^{-5}. The constants of the fatty acids (excepting formic acid, which is quite strong) all lie between 1.2×10^{-5} and 1.8×10^{-5}, acetic acid having the latter value. It should therefore, be possible to titrate, with analytical accuracy, all such acids. This conclusion is fully confirmed by common experience. Phenolphthalein is consequently an excellent indicator for almost all acids, including the so-called weak acids.

The results to be expected in the titration of a weak base, MOH, by means of a strong acid may be calculated in an analogous manner. In this case $M \times OH = k_b MOH$,

and
$$\frac{OH}{k_b} = \frac{MOH}{M}.$$

After the addition of acid to the solution of the base until the disappearance of color indicates neutrality, the fraction MOH/M expresses the error, E_b, of the titration. Since $OH = 10^{-6}$.

$$k_b = 10^{-6}/E_b. \qquad (5)$$

For an error of 0.1 per cent, k_b should be equal to 10^{-3}; for 0.2 per cent, 0.5×10^{-3}. The ionization constants of 30 organic bases have been measured by Bredig.[1] In addition to very strong bases of the quaternary ammonium type, 21 others were studied. Only four of these have constants over 10^{-3}. These are diethylamine, dipropylamine, coniïn, and piperidine. These could be titrated accurately with phenolphthalein as indicator. Thirteen more, mostly aliphatic amines, have constants between 10^{-3} and 0.5×10^{-3}. These could be titrated with a fair degree of accuracy. The constant for ammonia is 0.023×10^{-3}. The error of titration would be about 4 per cent. In the last experiments of Tables II. to V. the solutions became colorless when the concentration of the free ammonia was about 4 per cent of the concentration of the salt. It is, of course, evident that this last fact was used in arriving at the above conclusions. By combining the equations representing the relation between ionization constants and errors of analysis we get for the case where $E_b = E_a$

[1] *Loc. cit.*

$$\frac{k_b}{k_a} = \frac{OH}{H} \qquad (6)$$

and for $k_b = k_a$

$$\frac{E_b}{E_a} = \frac{OH}{H}. \qquad (7)$$

The first of these equations shows that for the same error of analysis of base and acid the ratio of the ionization constants of base and acid must be the same as that of the minimum detectable concentrations of hydroxyl and hydrogen. The second equation shows that if base and acid have equal ionization constants, the errors of analysis are in the same ratio as that of minimum detectable hydroxyl to hydrogen. The equations are applicable to indicators in general. The ratio OH to H will be characteristic for each indicator. For phenolphthalein it has been shown to be about 80. It is well known that this substance is a poorer indicator for weak bases than for weak acids. The quantitative relationship is given by these equations. While for the accurate titration of the weakest bases phenolphthalein could not be used as an indicator, it could be so used with many of the amines and other moderately weak bases.

Since it is possible by means of phenolphthalein to detect hydroxyl in concentration as small as 10^{-6}, it should be found that those alkali or alkali earth salts of weak acids, which by hydrolysis, give solutions exceeding in alkalinity this minimum hydroxyl concentration, should be alkaline toward phenolphthalein. Sodium acetate in decinormal solution is hydrolyzed to the extent of 0.01 per cent.[1] In this solution $OH = 10^{-5}$. Experiment 3, Table V, shows that 100 cc. of such a solution, plus 0.05 cc. N/10 phenolphthalein, should have a color equivalent to that produced by 8 cc. of N/20,000 phenolphthalein contained in 100 cc. of alkaline water. An experiment made with pure, carefully recrystallized, sodium acetate, gave a result in harmony with this deduction. The color of the solution was distinctly red. Lellmann[2] proposed the use of phenolphthalein to determine the relative affinities

[1] Shields : Ztschr. phys. Chem., **12**, 184 (1893).
[2] Ber. d. chem. Ges., **22**, 2101 (1889).

of weak acids, but has not used it[1] on account of its extreme weakness as an acid and the possibility of complications which might arise from the presence of the phenol groups. However, the method may be of some use as a means of determining rapidly the approximate affinities of acids whose salts are slightly hydrolyzed.

In the case of salts of weak dibasic acids, I have shown[2] that the degree of hydrolysis is much less than one might expect from the conductivity of the free acid.[3] The hydroxyl concentration of a decinormal solution of sodium bicarbonate is 3×10^{-6} (this is but 1/20 of the value calculated in the ordinary way from the conductivity measurements of carbonic acid). A hydroxyl concentration of 10^{-6} is the minimum detectable by means of phenolphthalein. In agreement with this Küster[4] has found as the result of very careful experiments that a *freshly made*, *dilute* solution of pure sodium bicarbonate is slightly alkaline toward phenolphthalein. (Owing to loss of carbon dioxide, such a solution becomes strongly alkaline on standing in an open vessel.[5]) I can confirm Küster's statement. The color of the solution is quite faint and depends upon the amount of the indicator used. The color may not appear if the water used be not free from carbon dioxide, or if an alcoholic solution of the indicator be employed, especially if the alcohol be not perfectly pure.

The Bleaching of Phenolphthalein by an Excess of Alkali.— It is well known that the addition of a very large excess of alkali to a slightly alkaline solution of phenolphthalein causes a great diminution in color. The results obtained in a series of experiments, made by mixing the indicator and sodium hydroxide in known amounts, are given in Table VII. Columns 2 and 3 give the concentrations used of phenolphthalein and sodium hydroxide respectively. In column 4 is given the volume of alkaline N/20,000 phenolphthalein required to match the color of the solution being studied. These figures

[1] Ann. Chem. (Liebig), 270, 204 (1892).
[2] This JOURNAL, 29, 452 (1903).
[3] Walker: Ztschr. phys. Chem., 32, 137 (1900).
[4] Ztschr. anorg. Chem., 13, 127 (1897).
[5] McCoy: *Loc. cit.*

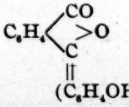
therefore represent the percentages of the red salt which have remained unbleached.

Table VII.

	10^3 Phenolphthalein.	10^3 NaOH.	N/20,000 Phenolphthalein. cc.	10^3 K_3.
1	50	1	56.0	12
2	50	5	15.0	9
3	50	10	7.3	8
4	50	20	3.1	6
5	50	50	1.1	6
			Mean,	8

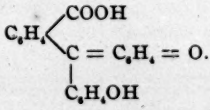
As a possible explanation of the bleaching, it may be supposed that the red salt is also an *extremely weak* acid, which is converted into the corresponding colorless salt only by the addition of a great excess of base. In such a case the value of $\frac{\text{acid} \times \text{base}}{\text{salt}}$ should be a constant. Here the red salt is the *acid* and the colorless body the *salt*. The results calculated on this basis are given in the last column.

A deeper insight into the nature of the whole problem of the action of bases on phenolphthalein may be obtained by considering the various reactions from the standpoint of the graphical formulas of this indicator and of its salts. Solid phenolphthalein is very probably a lactone.[1]



L

while the red salt and its corresponding free acid are quinone derivatives of the constitution

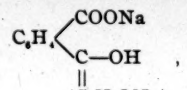


HQ

[1] Bernthsen : *Loc. cit.;* Nietzki and Burckhart : *Loc. cit.*

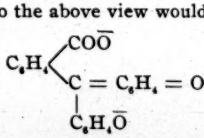
In aqueous solution the lactone, L, and the quinone carboxylic acid, HQ, would exist in equilibrium. The free acid, in turn, would be in equilibrium with its ions. For these reactions we should have as the obvious dynamic equations :[1] $L = k_1HQ$ and $H \times Q = k_2HQ$ (considering only the ionization of the carboxylic acid group), and therefore $H \times Q = k_1k_2L = K_1L$, where $K_1 = k_1k_2$. The value of K_1 has been found to be 7.5×10^{-11}. k_2 is the ionization constant of a substituted benzoic acid. The constant of benzoic acid is 6×10^{-5} and it may be supposed that k_2 is of the same order. If so, k_1 is equal approximately to 10^{-6}. This would mean that the concentration of the molecular quinoid carboxylic acid, HQ, is but one-millionth of that of the lactoid form.

The evidence for the constitution of the colorless salt, formed by the action of a great excess of sodium hydroxide, is of an indirect nature, but leads to the structural formula



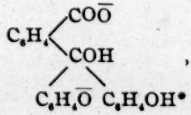
I

which represents a carbinol derivative. In this colorless salt the chromophoric quinone group is thought to be absent. In dilute solution the red salt would exist chiefly as ions, Q, which according to the above view would be



Q

The formation of the carbinol derivative from this is to be represented by the equation, $Q + H_2O \rightarrow HC$, where HC represents



HC

[1] Stieglitz : *Loc. cit.*

the carbinol ion-acid corresponding to the colorless salt. The body, HC, being an acid, due to the hydrogen atom, H*, we should have HC $\rightleftarrows$ C + H. The corresponding dynamic equations are $HC = k_3Q$ and $C \times H = k_4HC$. Therefore, $C \times H = k_3k_4Q = K_2Q$, where $K_2 = k_3k_4$. In other words Q would be a pseudo-acid[1] and its salts would have a hydrolysis constant, K_2, equal to K_{H_2O}/K_2. The value of K_2 has been found to be 8×10^{-3} (Table VII.). Therefore $K_2 = 1.5 \times 10^{-12}$. k_4 is the ionization constant of a substituted phenol. For the common phenol Walker and Cormack[2] have found the ionization constant to be 1.3×10^{-10}. If k_4 is of the same order, as is likely the case, k_3 would be about 10^{-2}. The equilibrium reactions of the bleaching are accordingly analogous to those representing the formation of the red salt: the equilibrium constant in each case is the product of two other constants. In the case of the formation of the red salt the equilibrium constant, k_1, is small and the ionization constant, k_2, comparatively large. In the other case the reverse is true: the equilibrium constant is large and the ionization constant is extremely small.

It would not have been possible to have carried out the work described in this paper, except for the fact that the bleaching reaction takes place very slowly. In Experiment 1, Table VII, the velocity of the change was roughly measured. After ten minutes the bleaching amounted to about 10 per cent; after fifty-four minutes to about 25 per cent; after twenty-four hours to 43 per cent; and after three days to 44 per cent. The alkaline phenolphthalein solutions used for the color comparison contained alkali of the same concentration as that used in this experiment. As these comparison solutions were made up only immediately before using, the fading which took place during the two or three minutes of use could be neglected. This observation on the velocity of bleaching clearly shows that we are dealing with a reaction which results in a condition of equilibrium, inasmuch as after the first day no further change occurred. The possibility of

[1] Hantzsch: Ber. d. chem. Ges., **32**, 579 (1899).
[2] J. Chem. Soc. (London), **77**, 5 (1900).

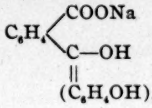
a non-reversible decomposition of the indicator is therefore excluded. In accord with this, it is found that upon diluting bleached solutions of phenolphthalein in concentrated alkali, the color becomes more intense. When the solution is neutralized with acetic acid and then immediately made slightly alkaline the solution has but a faint pink tint; but if the acid solution be boiled and then made slightly alkaline the intense red color appears. Green[1] thinks that this is evidence that the cause of the change of color is intramolecular instead of essentially ionic. I have carried out an experiment which throws additional light on this question. About 0.1 gram of pure phenolphthalein was dissolved in 10 cc. of N sodium hydroxide. After standing until equilibrium was reached, the deep-red solution was rendered just colorless by the addition of acetic acid. A slight precipitate formed, but much the larger part of the substance remained in solution. On standing at room temperature the colorless, and therefore *neutral* solution soon became somewhat red, the color gradually growing more intense; after an hour or two the solution was deep red. A considerable volume of dilute acetic acid was then required to again neutralize the solution, the unchanged phenolphthalein itself serving as indicator.

The result just described is welcome confirmatory evidence of the views here expressed on the constitutions of phenolphthalein derivatives, and on their dynamic relationships. The change of Q into HC takes place slowly, as the fading experiments show. The action is reversible and reaches a state of equilibrium. As has been said, a red solution of phenolphthalein, in dilute sodium hydroxide, probably contains the salt of a carboxylic acid of constitution HQ. Now aromatic carboxylic acids, in general, are *not* extremely weak acids. They are stronger than acetic acid. But in this case, owing to the fact that the corresponding free acid can go practically *instantaneously* and almost completely into the lactone, the *observed* properties are those of a very weak acid whose ionization constant is the product of k_1 and k_2.

On the other hand, the colorless salt, formula I, is also the

[1] Ztschr. f. Farb. u. Tex. Chem., 1, 413; Chem. Centrbl., 1902, II, 683.

salt of a carboxylic acid, but in this case the reversion to the tautomeric form *takes place slowly;* that is to say, the change, Q ⇄ HC does *not* take place instantly. It should, therefore, be possible, under favorable conditions, to observe properties characteristic of an aromatic carboxylic acid. Upon adding acetic acid to the strongly alkaline, bleached solution, until it became colorless, a neutral solution was obtained, which, on standing, became strongly alkaline. The neutral solution must have contained the salt of a moderately strong acid. The alkaline solution, spontaneously formed from the preceding, contained the ordinary red salt of phenolphthalein. The neutral salt was probably



II

But if this substance can transform *slowly* into the salt of HQ, which acid is *practically very weak*, the results obtained are easily understood. The solution of the latter salt would, of course, owing to hydrolysis, be strongly alkaline. Further, as a result of the competition of the phenol groups of II, a portion of the alkali of the salt of HQ would neutralize the former and thus convert II partly into I. This would tend to diminish the velocity of transformation of II into the red quinoid form (salt of HQ).

CHICAGO, January, 1904.

THE HYDROLYSIS OF ETHYL BUTYRATE BY LIPASE.

BY J. H. KASTLE, MARIUS EARLY JOHNSTON, AND ELIAS ELVOVE.[1]

During the summer of 1900, an experimental study of the action of lipase on certain ethereal salts was carried out in this laboratory by Loevenhart and one of us. The results of this investigation have already been published in this JOURNAL.[2] Among other things it was found that as compared with other

[1] Research Assistant in the Carnegie Institution of Washington.

[2] This JOURNAL, 24, 491–525.

ethereal salts, ethyl butyrate is very easily hydrolyzed by lipase, so readily in fact as to render it an exceedingly useful substance in the investigation of a number of problems connected with the action of this ferment.

Clear Solutions of Lipase.

It was also observed in our earlier work that filtration greatly diminishes the activity of the enzyme. To such an extent was this found to occur that at that time no attempts were made to obtain the ferment in anything like a condition of purity, nor even in the form of water-clear solutions. It was apparent, however, even from the outset, that clear and homogeneous solutions of the enzyme must be obtained before we could hope to accurately investigate certain phases of the lipolytic process. Some time after this, in studying the conduct of acids towards lipase, it was observed by Kastle and Hardin[1] that when 10 per cent extracts of hepatic lipase were allowed to stand with small amounts of N/100 hydrochloric acid a certain amount of proteid is coagulated, and when this extract is filtered, a clear, yellowish filtrate is obtained, which is found to possess considerable lipolytic activity. Upon this observation is based the following methods for the preparation of clear solutions of hepatic lipase :

Ten grams of fresh hog liver were thoroughly macerated with coarse white sand and made up to 100 cc. with water, and strained through a linen cloth. Twenty cc. of this extract were then diluted with 72 cc. of water and to the diluted extract 8 cc. of N/100 hydrochloric acid were added, and the mixture heated to 40° C. Under these conditions a heavy albuminous precipitate was thrown down. This was then filtered off and a clear filtrate obtained, having a light, golden-yellow color. The lipolytic activity of this solution before and after filtration was tested in the following manner :

Four tubes were prepared, two containing 5 cc. of the unfiltered solution and two containing 5 cc. of the filtered solution. To each of the tubes 0.1 cc. of toluene was added as antiseptic, and the tubes were heated on the water-bath at 40°

[1] Unpublished results of Kastle and Hardin.

C. for five minutes. 0.26 cc. of ethyl butyrate was then added to each tube, after which the tubes were allowed to remain in the bath for fifteen minutes. They were then removed from the bath and placed in ice-water and titrated with N/20 caustic soda with the following results :

	N/20 NaOH required.	Percentage of hydrolysis.
Unfiltered solution	5.05	12.67
" "	5.25	13.1
Filtered "	2.75	6.89
" "	3.00	7.53

From this it will be observed that in the preparation of clear lipase solution there is a falling off in activity of nearly one-half as compared with the original extracts. However, the activity of such clear solutions is still considerable, and the advantages of such solutions over the turbid aqueous extracts for the purposes of chemical study can scarcely be overestimated. In order to determine the amount of solid matter in these clear solutions of lipase, 5 cc. of such a solution were evaporated to dryness in a platinum dish over the water-bath, and dried to constant weight in the air-oven at 100° C. The residue was found to weigh 0.0104 gram. The residue was then ignited and weighed again. The mineral matter was found to weigh 0.0016 gram. It will be observed, therefore, that even on the assumption that the whole of the organic matter consists of lipase, and this is by no means probable, it can hydrolyze twice its weight of ethyl butyrate in fifteen minutes at 40° C. In view of the fact that clear solutions of lipase are less active than the unfiltered extracts from which they are prepared, it occurred to us to test the lipolytic activity of the residue after filtration. Accordingly, two 1-gram portions of the residue left, after filtering the above solution, were weighed out, and to one of these 100 cc. of distilled water were added, and to the other 100 cc. of a 0.2 per cent solution of sodium carbonate. These mixtures were then allowed to stand three days, at the end of which time they were filtered and their lipolytic activity tested in the usual manner. Tubes were prepared containing 10 cc. of the lipase solutions and 0.1 cc. of toluene. These were heated on the water-bath

for ten minutes at 40° C., and 0.26 cc. of ethyl butyrate was added to each tube. The tubes were then put back in the bath at 40° C. for fifteen minutes, at the end of which time they were placed in the ice-bath and titrated with N/20 caustic soda with the following results:

	N/20 caustic soda required. cc.	Percentage of hydrolysis.
Aqueous solution	0.51	1.28
0.2 per cent sodium carbonate solution	4.9	12.38

It is apparent from these results that the lipase contained in the residue left after precipitation with acid is comparatively insoluble in water, but is readily soluble in very dilute alkalies. The remarkable activity of the sodium carbonate extract as compared with the aqueous solution, together with the further fact that the alkaline solution also filters comparatively easily, led ultimately to the following methods for the preparation of clear solutions of lipase. Ten grams of fresh liver were thoroughly macerated with coarse white sand and made up to 500 cc. with water and 50 cc. of N/100 hydrochloric acid. The mixture was well shaken and allowed to stand over night. It was then filtered and the residue treated with 500 cc. of a 0.2 per cent solution of sodium carbonate. The activity of the two solutions was then tested in the usual manner: Temperature 40° C.; quantity of ethyl butyrate used, equal to 0.26 cc., and 0.1 cc. of toluene as antiseptic; time, fifteen minutes. The following results were obtained:

	N/20 NaOH required. cc.	Percentage of hydrolysis.
5 cc. acid solution of lipase, filtered	2.05	5.14
5 cc. of alkaline lipase, unfiltered	5.3	13.35

The sodium carbonate extract was then filtered and a clear reddish solution obtained. The lipolytic activity of this was tested at once, after which it was mixed with an equal volume of the hydrochloric acid solution described above, and the activity of the mixture was then tested, using 5 cc. of the

lipase solution, 0.26 cc. ethyl butyrate, 0.1 cc. of toluene, at 40° C. Time, fifteen minutes. The following results were obtained:

	N/20 NaOH required. cc.	Percentage of hydrolysis.
Acid solution of lipase	2.33	5.86
Alkaline solution of lipase	5.25	13.22
Mixed solution of lipase	4.3	10.83

These are the most active clear solutions of the lipolytic ferment that we have thus far been able to prepare. It has been found, however, that while very active, these clear solutions of lipase prepared by the use of sodium carbonate gave a heavy coagulum during the progress of hydrolysis, this being due, of course, to the coagulation of proteid matter by the butyric acid formed during the hydrolysis. Such, however, is not the case with the clear solutions of the ferment prepared by the use of very dilute acids, and hence the latter have been used altogether in our late work in studying the conduct of the enzyme toward ethyl butyrate.

It has also been found advantageous to employ butyric acid rather than hydrochloric in the preparation of clear solutions of the enzyme, the following method of preparation being finally adopted:

One gram of fresh hog liver is thoroughly macerated with powdered glass or coarse white sand and mixed with 75 cc. of water. The mixture is then heated to 35° C., and 5 cc. of N/10 butyric acid are added gradually and the mixture made up to 100 cc. with water. A heavy precipitate is formed which is filtered off by bringing the material on a folded filter. The filtrate, which has frequently been obtained without a vestige of color, is always perfectly clear and is usually slightly yellowish in tint. Five cc. of the clear extract prepared in this way has been found to hydrolyze from 5 to 6.25 per cent of ethyl butyrate in fifteen minutes at 40° C. when allowed to act on 0.26 cc. of the ethereal salt. In order to form some idea of the actual amount of lipase in the clear solutions prepared by means of N/10 butyric acid, 5 cc. of one

of these extracts were evaporated to dryness on the water-bath and dried in the air-oven at 110° C. to constant weight. The residue weighed 0.0047 gram; in other words, these clear solutions cannot contain more than 5 milligrams of the ferment in 5 cc., and yet, as has already been pointed out above, this amount of the ferment can hydrolyze 0.0145 gram of ethyl butyrate, in fifteen minutes, under the general conditions employed in our experiments. In order to form some idea of the quantity of ethyl butyrate which this amount of lipase could hydrolyze in longer intervals the following experiment was tried: Five cc. of a clear solution of lipase which had been prepared on Dec. 30, 1902, were mixed with 0.26 cc. of ethyl butyrate and put in the incubator at 40° C. at 4 P. M., Dec. 30. After twenty-four hours, it required 10.3 cc. N/20 caustic soda to neutralize the butyric acid formed. It was then put back in the incubator at 40° C. for another twenty-four hours, at the end of which time it required 13.25 cc. N/20 caustic soda. A second portion of ethyl butyrate, 0.26 cc., was then added, when it was again placed in the incubator, where it remained until 10.30 A. M., Jan 4, 1903. It was found at this time to require 28.2 cc. N/20 caustic soda to neutralize the acid produced. Altogether, therefore, an amount of ethyl butyrate corresponding to 51.5 cc. N/20 caustic soda had been hydrolyzed in eighty-nine and a half hours; hence an amount of lipase not exceeding 5 milligrams, and probably much less, had hydrolyzed nearly 300 milligrams of ethyl butyrate, or about sixty times its own weight of the ethereal salt, and yet at the end of this interval the ferment was practically as active as it was at the beginning of the experiment. Since the butyric acid produced considerably retards the hydrolysis, the quantity of ethyl butyrate hydrolyzed is certainly much less than that which would have been transformed had it been possible to remove the acid as fast as it was produced, or even if it had been neutralized as fast as formed. It should also be borne in mind that in all probability the 5 milligrams of total solids left on evaporating 5 cc. of the clear lipase solution did not consist entirely of the enzyme.

The Stability of Clear Solutions of Lipase.

It has been shown by Kastle and Loevenhart that, in perfectly dry condition, lipase is a stable substance. A mixture of fresh hog pancreas and sand, for example, that had been prepared and dried in the air on July 12, 1900, was found to be capable of hydrolyzing ethyl butyrate on Nov. 15, 1901. On the other hand, it was found that the ordinary aqueous extracts of the liver and pancreas soon lose their lipolytic power even when preserved under mild antiseptics, such as toluene and thymol. The clear solutions prepared by means of acids, however, have been found to be much more stable. Under the conditions ordinarily prevailing in the laboratory, they may be preserved for weeks and even months without exhibiting any marked falling off in lipolytic activity. This in itself is a great convenience, and seems to be due, in part at least, to the fact that small amounts of acid protect the solution of the ferment against putrefactive changes. Larger quantities of the acid, on the other hand, have been found to destroy the enzyme completely. Some idea of the stability of these clear solutions of the ferment and the preservative action of dilute acids may be obtained from an examination of the following data:

Five cc. of a 10 per cent liver extract were mixed with 19 cc. of water and 1 cc. of N/100 hydrochloric acid on October 21, 1902. The activity of the mixture was tested immediately and also after standing a certain interval, by allowing 5 cc. of it to act on 0.26 cc. ethyl butyrate for fifteen minutes at 40° C. The results of these measurements are as follows:

Date of test.	Amount of ethyl butyrate hydrolyzed. Gram.
Oct. 21, 1902	0.02552
" 27, 1902	0.02900
March 29, 1903	0.02378

It will be observed, therefore, that the solution had only lost 7 per cent of its lipolytic activity in five months. The increase in hydrolyzing power, observed after standing six days, is interesting, and is doubtless due to the liberation of

small amounts of lipase from its zymogen by the action of the dilute acid. Similar results have been obtained in the case of other soluble ferments by other observers. Similarly it has been found that clear solutions of the ferment prepared by precipitating its aqueous extracts with butyric acid are also quite stable, as may be seen from the following :

A clear solution of lipase was prepared on Jan. 28th by precipitating 100 cc. of a 1 per cent extract of liver in a 0.2 per cent solution of sodium carbonate with 15 cc. N/10 butyric acid, and filtering. A small amount of thymol was added to the clear filtrate. The activity of this solution was then tested immediately by allowing 5 cc. of it to act upon 0.26 cc. ethyl butyrate for fifteen minutes at 40° C. Under these conditions 5 cc. of the clear solution were found to hydrolyze 7.25 per cent of the ethyl butyrate. In order now to test the stability of this solution two tubes, each containing 5 cc. of the solution, were hermetically sealed and kept in a dark closet for eighty-three days at ordinary room temperature. At the end of this time the tubes were opened and their lipolytic activity tested in the usual manner. It was found that in one case 7.3 per cent of ethyl butyrate had been hydrolyzed in fifteen minutes at 40° C., whereas, in the second case, 7.25 per cent of the ethereal salt had been decomposed. It is apparent, therefore, that this clear solution of lipase had suffered no diminution in activity during the eighty-three days that it had been kept in sealed tubes. Similar results have been obtained with other clear solutions of lipase prepared by the action of acids on the aqueous extracts of the liver, indicating that very small amounts of acid exercise a preservative action on this enzyme.

On the Effect of Filtration through a Porous Cup on the Activity of Clear Solutions of Lipase.

It has been observed that the activity of clear solutions of lipase is not diminished even by repeated filtrations through ordinary filter-paper. In studying the effect of various filtering media on the activity of solutions and extracts of the ferment, it has been found, however, that filtration through a

Pasteur-Chamberland filter completely removes the enzyme, even from its clear solutions. That such is the case may be seen from the following data :

A clear neutral solution of hepatic lipase was divided into two portions, one of which was filtered through a porous cup, while the other was preserved in its original condition. Both the filtered and unfiltered solutions were then tested towards ethyl butyrate in the usual manner, using 5 cc. of the extract and 0.26 cc. ethyl butyrate. Time, fifteen minutes; temperature, 40° C., with the following results :

	N/20 NaOH required. cc.	Amount of ethyl butyrate hydrolyzed. Gram.
Original solution	1.8	0.0104
Filtrate from porous cup	0.1	0.00058

In a second experiment, we obtained the following :

	N/20 NaOH required. cc.	Amount of ethyl butyrate hydrolyzed. Gram.
Original solution	1.6	0.00928
Fltrate	0.15	0.00087

It is apparent, therefore, that animal lipase belongs to the class of ferments that are retained by the walls of the porous cup.

The Kinetics of the Lipolytic Process.

In our earlier work on lipase, Loevenhart and one of us (Kastle) studied the effect of the concentration of the ethereal salt on the velocity of the hydrolysis, using ordinary aqueous extracts of the ferment. The coefficient of velocity was not observed to be constant, but showed a more or less regular falling off from the highest values obtained for short intervals of time. This retardation is doubtless to be explained by the fact that the acid liberated during the progress of the reaction exerts an inhibiting action on the ferment, and any other irregularities in our first values are doubtless to be explained by the more or less imperfect methods of investigation which were then employed, such as the use of an aqueous extract of the ferment, the constancy and homogeneity of which could not al-

ways be relied upon, and, secondly, the employment of larger amounts of ethereal salt than could be gotten into solution under the conditions of the experiment. It was determined, however, with reasonable exactness that for a given amount of the ferment the quantity of ethyl acetate and ethyl butyrate hydrolyzed in a given time was practically independent of the initial concentration of the ethereal salt.

Having obtained clear and uniform solutions of animal lipase, by the methods already described above, we were now in a better position to study the kinetics of the lipolytic process. In order, however, to make the necessary measurements, it was as essential to employ a solution of the ethereal salt, rather than a mixture thereof with water, as it was to make use of a solution of the ferment, rather than a turbid extract thereof. It was in this connection that the attempt was made originally to employ an alkali salt of one of the acid ethers, which as a class are characterized by great solubility in water. Unfortunately for our present purpose, it was found that lipase is unable to effect the hydrolysis of this class of substances. The results of this part of the investigation have already been published in this JOURNAL.[1] Such having proved to be the case, recourse was had to a dilute solution of ethyl butyrate, as the substance on which to make the necessary measurements. It was found that by vigorous shaking 1.2 cc. of pure ethyl butyrate, equal to 1.0931 grams, could be dissolved in a little less than 200 cc. of water. This very nearly represents the maximum solubility of this ester in water. The solution employed in our first measurements was prepared by vigorously agitating this amount of the ethereal salt with the required amount of water and making up the solution to a total volume of 200 cc. A solution containing 1 cc. of ethyl butyrate, 0.9109 gram, in a total volume of 200 cc., was also frequently employed. The strength of such solutions was determined by saponifying a known amount of the given solution with caustic soda, and also by completely hydrolyzing a known amount of it by means of lipase itself. The two methods not only gave numbers closely agreeing

[1] This JOURNAL, 27, 481–486.

among themselves but also with the theory for the given amount of ethyl butyrate employed. This agreement was found to be so close, in fact, that in what follows the concentration of the solution of the ethereal salt is the calculated value for the particular solution employed. The clear solution of lipase employed in this part of the work was prepared by macerating 1 gram of fresh hog liver with coarse white sand. Seventy-five cc. of water were then added and the extract thus obtained was heated to 35° to 40° C. and precipitated with 5 cc. N/10 butyric acid. The solution was then made up to 100 cc. and filtered through a folded filter. A clear, golden-yellow solution of lipase was thus obtained. In many of our experiments this was employed directly, making the necessary correction for the initial acidity of the solution which was determined in every case. In many series of experiments, however, the clear lipase solution was first neutralized by means of standard caustic soda. In this manner all corrections for initial acidity of the extract were obviated. In our earlier work on lipase, Loevenhart and one of us (Kastle) found litmus to be by far the most satisfactory indicator. With the clear solution of the ferment, however, it by no means compares with phenolphthalein in point of delicacy, hence the latter has been used exclusively in this part of the work. With the view of determining the coefficient of velocity of the hydrolysis of ethyl butyrate by lipase, the following series of experiments were carried out, under slightly varying conditions, in the way of concentration, temperature, and time. Under each series of experiments will be found the exact conditions that obtained for that particular series.

Series I.

Conditions.—Fifty cc. ethyl butyrate solution, containing 1.0931 grams of ethyl butyrate in 200 cc., 50 cc. lipase, 5 cc. of which had an initial acidity equivalent to 0.45 cc. N/20 caustic soda. The solutions were mixed and allowed to stand for the several intervals indicated below at 21° C. At the end of each interval, 10 cc. of the mixture were removed from the flask by means of a pipette and titrated with N/20 caustic soda

deducting the initial acidity of the lipase from the amount required in each case. The value of the titer, in terms of the caustic soda employed, was found to be equivalent to 4.71 cc. for complete hydrolysis. This is the value of a[1] in the equation, $C = \frac{1}{t} ln. \frac{a}{a-x}$.

Time in minutes.	N/20 caustic soda required. cc.	C.
30	0.95	0.00751
64	1.45	0.00575
97	1.80	0.00496
132	2.25	0.00492
204	2.90	0.00469

Same as above except that the intervals were longer.

Time in minutes.	Caustic soda required. cc.	C.
60	1.30	0.00538
121	2.05	0.00472
198	2.75	0.00443
361	3.50	0.00376
467	3.80	0.00352

Series II.

Conditions.—Fifty cc. of ethyl butyrate solution were mixed with 25 cc. of neutral lipase solution and 25 cc. of water. The mixture was allowed to stand for the several intervals indicated below, at the end of which time 10 cc. of the mixture were removed by means of a pipette and titrated with N/20 caustic soda. Temperature 22°.5 C., $a = 3.86$.

Time in minutes.	Caustic soda required. cc.	C.
15	0.45	0.00827
30.5	0.70	0.00656
48.5	1.00	0.00618
63.5	1.10	0.00528
78.5	1.25	0.00498
100.5	1.55	0.00519
133.5	1.80	0.00470
197.5	2.30	0.00467
266.0	2.70	0.00452

[1] In what follows the value of the whole titer, namely, a, is given for each series of experiments, in terms of the particular solution of sodium hydroxide employed in any given series of experiments. In this way the necessary correction has been made for any slight variation in the concentration of the sodium hydroxide, from the strength indicated in the tables.

Series III.

Conditions.—Twenty-five cc. ethyl butyrate solution were mixed with 10 cc. neutral lipase and 215 cc. of water. The mixture was allowed to stand for the required intervals at 22° C. Fifty cc. of the mixture were pipetted off at the end of each interval and titrated with N/50 caustic soda. In this series of experiments $a = 9.905$.

Time in minutes.	N/50 NaOH required. cc.	C.
15	0.53	0.00369
30	0.87	0.00307
46	1.15	0.00268
61	1.45	0.00259
76	1.75	0.00256

Series IV.

Conditions.—Twenty-five cc. ethyl butyrate solution were mixed with 10 cc. neutral lipase and 465 cc. of water, and the mixture allowed to stand for the desired intervals at 20° C. At the end of the several intervals, 50 cc. were removed by means of a pipette and titrated with N/100 caustic soda. In this series of experiments $a = 9.905$.

Time in minutes.	N/100 NaOH required. cc.	C.
16	0.65	0.00424
31	0.90	0.00307
46	1.35	0.00318
61	1.45	0.00259
91	1.98	0.00244
121	2.35	0.00224
151	2.75	0.00215
181	3.25	0.00219

In this connection we desire to call attention to the results of the several series of observations given under the head of the effect of temperature on the velocity of the hydrolysis (p. 540). In general, the results therein enumerated are altogether similar to those given in Series 1 to 4, inclusive. In this connection, however, it will be observed, under the head of the effect of temperature on the velocity of the reaction, that in Series 3 at 20° C. and in Series 5 at 40° C.

much more constant values for the coefficient of velocity have been obtained. In fact, in these two series of experiments the several values of C as calculated from the equation

$$C = \frac{1}{t} ln. \frac{a}{a - x},$$

are sufficiently concordant to indicate that the reaction under consideration is monomolecular. Taken collectively, however, it will be observed that the several values of C for any particular series show a slight, or sometimes considerable, falling off from the first value thereof, indicating a somewhat higher initial rate of hydrolysis than that which obtains for subsequent intervals. It seemed probable that this gradual retardation of the hydrolysis was brought about by the inhibiting action of the acid produced during the hydrolysis. That such is the case is apparent from the following experiments:

In order to determine the effect of free butyric acid on the progress of the hydrolysis, two experiments were tried. A mixture, No. 1, was made, containing 5 cc. of neutral lipase, 10 cc. of ethyl butyrate, and 35 cc. of water, and a second, No. 2, was prepared containing 5 cc. of neutral lipase, 10 cc. of ethyl butyrate, 3 cc. of N/50 butyric acid, and 32 cc. of water. These solutions, Nos. 1 and 2, were allowed to stand at 22° C. for the several intervals indicated below, at the end of which the entire solutions were titrated with N/50 caustic soda, making allowance, of course, for the caustic soda used in neutralizing the free butyric acid in Experiment 2, at the end of the first interval. The several amounts of caustic soda required, together with the several values of C calculated for each interval separately, are given below. $a = 19.81$.

Experiment 1.

Time in minutes.	N/50 caustic soda required. cc.	C.
15	1.6	0.00561
15	1.15	0.00433
15	1.1	0.00443

Experiment 2.

Time in minutes.	N/50 caustic soda required. cc.	C.
15	1.125	0.00390
15	1.15	0.00422
15	1.1	0.00431

Similar experiments were tried with N/50 hydrochloric acid. Two experiments were set up: No. 1 contained 5 cc. neutral lipase, 10 cc. ethyl butyrate, and 35 cc. water. No. 2 contained 5 cc. neutral lipase, 10 cc. ethyl butyrate, 3 cc. N/50 hydrochloric acid, and 32 cc. water. These were allowed to stand for the several intervals indicated below at a temperature of 25° C., and the whole solution was titrated at the end of each interval, due allowance being made for the caustic soda required by the N/50 hydrochloric acid originally present in No. 2. $a = 19.81$.

Experiment 1.

Time in minutes.	N/50 caustic soda required. cc.	C.
15	1.55	0.00543
15	1.35	0.00512
15	1.30	0.00533

Experiment 2.

Time in minutes.	N/50 caustic soda required. cc.	C.
15	0.65	0.00223
15	1.4	0.00505
15	1.3	0.00507

The following are the results of another series of experiments showing the effect of N/50 hydrochloric acid on the rate of hydrolysis of ethyl butyrate by lipase:

Experiment 1.

Conditions.—Five cc. neutral lipase, 10 cc. ethyl butyrate, 35 cc. water. Temperature 22° C. $a = 19.81$.

Time in minutes.	N/50 caustic soda required. cc.	C.
15	1.4	0.00489
15	0.95	0.00352
15	1.05	0.00412

Experiment 2.

Conditions.—The same as those given under Experiment No. 1, except that 3 cc. of N/50 hydrochloric acid and 32 cc. of water were employed instead of 35 cc. of water, $a = 19.81$.

Time in minutes.	N/50 caustic soda required. cc.	C.
15	0.6	0.00205
15	1.00	0.00357
15	1.10	0.00417

It is evident from these results that the presence of free acid, either hydrochloric or butyric, greatly diminishes the velocity of the reaction during the first interval. It is interesting to note, however, that the several coefficients of velocity obtained for the successive intervals are practically the same in all cases, indicating that the effect of these small quantities of free acid on the ferment is purely a temporary one. In general it may be said that small amounts of free acid greatly inhibit the action of the enzyme but do not permanently destroy its activity. On the other hand, we have observed in other experiments that larger amounts of acids completely destroy the ferment.

Determination of the Order of the Lipolytic Reaction by van't Hoff's Method.

In order to determine the precise nature of the change here under consideration we have made use of van't Hoff's method, which depends upon the effect of change of concentration on the velocity of the reaction. This was carried out in the following manner: 10 cc. of neutral lipase were mixed with 25 cc. of ethyl butyrate and 15 cc. of water. The total of 50 cc. represents the unit of volume. This was allowed to stand for thirty minutes at 20° C. Ten cc. of the mixture were then removed by means of a pipette and the free acid determined by means of N/100 caustic soda. It required 1.3 cc. of N/100 caustic soda. Simultaneously with the removal of the 10 cc. employed in the titration, the remainder of the original solution, 40 cc., was made up to a total volume of 90 cc. with water and kept for another interval of thirty minutes under exactly

the same conditions of temperature, etc., as before. At the end of this time, 20 cc. of the second mixture were drawn out by means of a pipette and the free acid determined, which required 2.25 cc. N/100 caustic soda. The ethyl butyrate solution employed was of such strength that if all of the 25 cc. originally used in the experiment had been hydrolyzed, the free acid produced would have required 99.05 cc. of the N/100 caustic soda employed. Representing by this number the original concentration, the concentration at the end of the first thirty minutes may be represented by 92.55, since $99.05 - (1.3 \times 5) = 92.55$. We may therefore tabulate these results as follows:

Time in minutes.	Concentration.
0	99.05
30	92.55
Mean concentration,	95.8

If now 92.55 cc. of N/100 caustic soda is the equivalent of 50 cc. of the mixture at the end of the first thirty minutes, the 40 cc. of the mixture remaining which had been diluted up to 90 cc. with water, contained an amount of ethyl butyrate equivalent to four-fifths of 92.55 cc. of N/100 caustic soda, namely, 74.04. If this amount was present in 90 cc., then 50 cc. of this, which was taken as the unit volume, contained at that time an amount of ethyl butyrate equivalent to five-ninths of 74.04, namely, 41.13. This last number, therefore, represents the concentration at the beginning of the second interval, and since 20 cc. of the mixture contained free acid equivalent to 2.25 cc. N/100 caustic soda, the total amount of acid present was equivalent to 10.125 N/100 caustic soda. Subtracting from this the amount of acid present at the beginning of the second interval, namely, $1.3 \times 4 = 5.2$, we get 4.925 cc. N/100 caustic soda as the equivalent of the total acid produced during the second interval, and in 50 cc. of this, the unit volume, there was produced during that time an amount of acid equivalent to five-ninths of 4.925 or very nearly 2.73 cc. N/100 caustic soda. Subtracting this from 41.13 we obtain the concentration at the end of the second interval,

namely, 38.40. Hence we have the following data for the second interval:

Time in minutes.	Concentration.
0	41.13
30	38.40
Mean concentration for the second interval,	39.765

Substituting these several values in van't Hoff's equation, we arrive at the number representing the order of the reaction under consideration:

$$n = \frac{\log \left\{ \frac{dC_1}{dt} : \frac{dC_2}{dt} \right\}}{\log (C_1 : C_2)} = \frac{\log \frac{dC_1}{dt} - \log \frac{dC_2}{dt}}{\log C_1 - \log C_2}.$$

$$\frac{dC_1}{dt} = \frac{99.05 - 92.55}{30} = \frac{6.5}{30} = 0.21667; \; C_1 = 95.8.$$

$$\frac{dC_2}{dt} = \frac{41.13 - 38.40}{30} = \frac{2.73}{30} = 0.091; \; C_2 = 39.765.$$

$$\log_e 0.21667 = -1.5294; \; \log_e 0.091 = -2.3969.$$

$$\log_e 95.8 = 4.5623; \; \log_e 39.765 = 3.6830.$$

$$\therefore n = \frac{-1.5294 - (-2.3969)}{4.5623 - 3.6830} = \frac{0.8675}{0.8793} = 0.986.$$

A second determination of N from other data gave 0.974.

There can be no doubt, therefore, that in the hydrolysis of ethyl butyrate by lipase we have to deal with a monomolecular process, which is influenced to a slight extent by one of the products of the change, namely, the acid. It has also been found that alcohol slightly retards the action of the ferment, but with the small quantities of this substance resulting from the hydrolysis of dilute solutions of the ethereal salt its effect is so slight as to be altogether negligible.

On the Effect of Temperature on the Rate of Hydrolysis of Ethyl Butyrate by Lipase.

In his "Études de Dynamique Chimique" van't Hoff[1] has

[1] "Études de Dynamique," van't Hoff's English Translation, 1896, page 125.

pointed out that in the greater number of cases thus far investigated, the ratio of the velocity constants of a chemical reaction for two temperatures differing by 10° C. has a value between 2 and 3 approximately. In other words, a rise of temperature of 10° C. doubles or sometimes trebles the velocity of a reaction. Among other examples, he cites the following:

Reaction.	Mean ratio of velocities at T and (T + 10).
Hydrolysis of ethyl acetate	1.89 and 2.03
" " acetamide	2.12
Inversion of cane-sugar	3.63
Hydrolysis of tertiary amyl acetate	2.19

It therefore occurred to us that it would be interesting to determine the velocity constants of the reaction under investigation, at several temperatures differing from one another by 10° C. Accordingly the rate of hydrolysis has been determined at 0° C., 10° C., 20° C., 30° C., and 40° C. The results of these measurements, together with all necessary data, are given in the following tables:

Series 1.

Quantities of Substances Employed.—Temperature 0° C.

10 cc. neutral lipase
25 cc. ethyl butyrate
15 cc. water
50 cc. total volume
Amount titrated at end of each interval, 10 cc.
$a = 19.81$

Time in minutes.	N/100 caustic soda required. cc.	C.
15	0.20	0.00068
30	0.45	0.00077
45	0.70	0.00080
60	0.80	0.00069
75	0.90	0.00062
	Average,	0.000712

Series 2.

Quantities of Substances Employed.—Same as in Series 1. Temperature 10° C.

Time in minutes.	N/100 caustic soda required. cc.	C.
15	0.45	0.00153
30	0.75	0.00129
45	1.05	0.00121
60	1.30	0.00113
75	1.60	0.00112
	Average,	0.001256

Series 3.

Quantities of Substances Employed.—Same as in Series 1. Temperature 20° C.

Time in minutes.	N/100 caustic soda required. cc.	C.
15	0.65	0.00223
30	1.35	0.00235
45	1.80	0.00212
60	2.2	0.00206
75	2.95	0.00215
	Average,	0.00218

Series 4.

Quantities of Substances Employed.—Same as in Series 1. Temperature 30° C.

Time in minutes.	N/100 caustic soda required. cc.	C.
15	1.15	0.00399
30	2.15	0.00383
45	3.10	0.00378
60	3.85	0.00360
75	4.60	0.00352
	Average,	0.00374

Series 5.

Quantities of Substances Employed.—Same as in Series 1. Temperature 40° C.

Time in minutes.	N/100 caustic soda required. cc.	C.
15	1.65	0.00580
30	3.15	0.00577
45	4.55	0.00580
60	5.75	0.00571
75	7.15	0.00597
	Average,	0.00581

From these results the following mean ratio of velocities for the reaction at the several intervals of temperature have been calculated. These are as follows :

Series compared.	Ratio of velocities at T and (T + 10).
1 and 2	1.76
2 and 3	1.74
3 and 4	1.71
4 and 5	1.55
Average,	1.69

The Catalytic Power of Lipase.

It has already been pointed out above that lipase can hydrolyze three times its weight of ethyl butyrate in fifteen minutes, or about sixty times its weight in eighty-nine and a half hours, when allowed to act upon an excess of the ethereal salt, under the conditions usually employed in the earlier part of our work on the ferment. A much better idea of the action of lipase as a catalyzing agent, however, can be gained from the following experiment: 10 cc. of neutral lipase were mixed with 10 cc. of ethyl butyrate solution. This mixture was allowed to stand at 22° C. for a certain interval and then titrated with N/20 sodium hydroxide, using the whole of the mixture as the titer. After neutralization the mixture was set aside and at the end of a second interval, its acidity was determined in the same way. The following are the results of the several titrations for the several intervals, using the whole of the solution in each titration. In calculating the several values of C., we have ignored the change in concentration of the original solution, due to the addition of the successive portions of caustic soda. This is permissible since

it has been shown that the amount of ethyl butyrate hydrolyzed is largely independent of the amount of water in which it is dissolved.

No. of intervals.	Total time in minutes.	N/20 sodium hydroxide required at end of each interval. cc.	Total volume N/20 NaOH required for given time. cc.	C. ($a = 7.71$.)
1	15	1.4	1.4	0.01336
2	32	1.5	2.9	0.01474
3	45	1.2	4.1	0.01686
4	60	1.3	5.4	0.02009
5	76	1.2	6.6	0.02550
6	91	0.8	7.4	0.03531
7	106	0.3	7.7	.....
8	120	0.15	7.85	.....
			Average,	0.02094

It will be observed that at the end of an interval of one hundred and twenty minutes all of the ethyl butyrate had been decomposed. In order, therefore, to determine whether the lipase in this solution had suffered any diminution in activity a second portion of ethyl butyrate solution, namely 10 cc., was added and the whole mixture titrated with N/20 sodium hydroxide at the end of certain intervals as before. The following are the results of the second series of titrations:

No. of intervals.	Total time in minutes.	N/20 sodium hydroxide required at end of each interval. cc.	Total volume N/20 NaOH required for given time. cc.	C. ($a = 7.71$.)
1	15	1.56	1.55	0.01496
2	32	1.65	3.20	0.01676
3	37	1.40	4.60	0.01932
4	62	1.25	5.85	0.01393
5	78	1.05	6.90	0.02889
6	99	0.60	7.50	0.03639
7	120	0.30	7.80	.....
			Average,	0.02321

We see, therefore, that at the end of the second series of measurements, namely, during an interval of one hundred and twenty minutes, just as much ethyl butyrate was hydrolyzed as during the first period of one hundred and twenty minutes. It would seem, therefore, that lipase suffers no permanent alteration while effecting the hydrolysis of the ethereal salt, but that it retains its complete activity regardless of the amount of substance that it has previously hydrolyzed. In this sense it belongs to the class of true catalyzing agents. The increase in the value of C in these two series of experiments and the slight increase of the values of C in the second series as compared with the first is probably due to the fact that lipase acts more rapidly in a neutral or slightly alkaline medium than in an acid one.

On the Influence of Concentration of the Ethyl Butyrate on Its Hydrolysis by Lipase.

Some of our earlier experiments seemed to indicate that the amount of ethyl butyrate hydrolyzed by lipase is within certain limits independent of the concentration of the ethereal salt. That such is the case may be seen from the following:

A series of six experiments was set up, using 5 cc. of a clear lipase solution and 5 cc. of a solution of ethyl butyrate (1.2 cc. of the compound in 200 cc.) in each experiment. The concentration was varied by the addition of the several amounts of water indicated below. The lipase was allowed to act for twenty hours at 18° C in each experiment.

No. of experiment.	Volume of water used. cc.	Concentration of ethyl butyrate per liter.	N/20 sodium hydroxide required. cc.	Percentage of ethyl butyrate hydrolyzed.
1	0	2.7328	3.40	72.18
2	10	1.3664	3.60	76.43
3	20	0.9109	3.50	74.31
4	30	0.6832	3.65	77.49
5	40	0.5466	3.65	77.49
6	50	0.4554	3.70	78.55

In a second series of experiments,[1] 1 cc. of a dilute solution of clear lipase and amounts of ethyl butyrate solution, varying from 1 cc. to 8 cc. were employed. The whole was then made up to a total volume of 10 cc. in each case, and the several mixtures kept at 40° C. for six hours, at the end of which time they were titrated with N/20 sodium hydroxide, with the following results:

No. of experiment.	Amount of ethyl butyrate in 10 cc.	V'l'me N/20 sodium hydroxide required.	Amount of ethyl butyrate hydrolyzed.	Perc'ntge of ethyl butyrate hydrolyzed.
	Gram.	cc.	Gram.	
1	0.0055	0.80	0.0046	83.6
2	0.0110	1.55	0.0090	81.8
3	0.0175	2.40	0.0140	80.1
4	0.0220	3.10	0.0180	80 1
5	0.0275	3.60	0.0210	76.0
6	0.0330	4.35	0.0254	77.0
7	0.0385	4.85	0.0283	73.6
8	0.0440	5.00	0.0292	66.3

In a third series of experiments designed to show the effect of concentration on the hydrolysis of the ethyl butyrate by lipase, 0.05 gram of the fresh liver tissue was employed in each experiment, together with 10 cc. of ethyl butyrate solution (1.2 cc. in 200 cc.), and at a total dilution of 10, 20, and 30 cc. The flasks containing these mixtures were kept at 21° C. for forty minutes, at the end of which time they were titrated with N/20 sodium hydroxide, with the following results:

[1] The results of this series of experiments would seem at first glance to indicate that the hydrolysis is directly proportional to the amount or ethyl butyrate present, may be seen, for example, by comparing Experiments 1, 2, and 3; but a more careful comparison of all of these results will show that this is true only in the case of very small amounts of the ethereal salt, as may be seen from a comparison of Experiments 1 and 8. This explains, therefore, why it is possible under certain conditions to increase the quantity of ethereal salt without causing any noticeable increase in the hydrolysis, as may be seen from Series 1, 2, 3, and 4 under this head.

No. of experiment.	Dilution.	Amount of ethyl butyrate present.	N/20 sodium hydroxide required.	Amount of ethyl butyrate hydrolyzed.	Percentage of ethyl butyrate hydrolyzed.
		Gram.	cc.	Gram.	
1	10	0.0550	1.8	0.0105	19.1
2	20	"	1.7	0.00993	18.5
3	30	"	2.3	0.0134	24.18

After the first titration the flasks were set aside and allowed to stand for three hours and forty-five minutes, at the end of which time they were titrated again with the following results:

No. of experiment.	N/20 sodium hydroxide required at end of second interval.	Amount of ethyl butyrate hydrolyzed during second interval.	Percentage of ethyl butyrate hydrolyzed during second interval.
	cc.	Gram.	
1	4.15	0.0242	44.00
2	3.90	0.0228	41.45
3	4.05	0.0237	43.09

With the view of throwing still further light on this point, four series of experiments were carried out with the following amounts of substances, under the following conditions:

1. Contained 5 cc. neutral lipase, 10 cc. ethyl butyrate solution (1 cc. in 200 cc.) and 10 cc. of water.

2. Five cc. of neutral lipase and 20 cc. of ethyl butyrate solution.

3. Five cc. of neutral lipase, 10 cc. of ethyl butyrate solution, and 40 cc. of water.

4. Five cc. of neutral lipase and 50 cc. ethyl butyrate solution.

These several solutions were allowed to stand at 19° C. At the end of fifteen-minute intervals, the whole of each solution was titrated with N/50 sodium hydroxide, with the following results:

Series 1.

$a = 19.81$.

No. of intervals.	Time in minutes.	N/50 sodium hydroxide required. cc.	C.
1	15	1.55	0.00543
2	30	2.75	0.00498
3	45	3.90	0.00487
4	60	5.05	0.00490
5	75	6.20	0.00501
6	90	7.30	0.00511
7	105	8.30	0.00517
		Average C_1,	0.00507

Series 2.

$a = 2 \times 19.81$.

No. of intervals.	Time in minutes.	N/50 sodium hydroxide required. cc.	C.
1	15	1.65	0.00283
2	30	2.95	0.00259
3	45	4.20	0.00249
4	60	5.35	0.00242
5	75	6.55	0.00241
6	90	7.80	0.00244
7	105	8.95	0.00244
		Average C_1,	0.00252

Series 3.

$a = 19.81$.

No. of intervals.	Time in minutes.	N/50 sodium hydroxide required. cc.	C.
1	15	1.80	0.00635
2	30	3.05	0.00557
3	45	4.30	0.00544
4	60	5.60	0.00554
5	75	6.85	0.00566
6	90	8.00	0.00575
7	105	9.20	0.00594
		Average C_1,	0.00575

Series 4.

$a = 5 \times 19.81.$

No. of intervals.	Time in minutes.	N/50 sodium hydroxide required. cc.	C.
1	15	2.00	0.00135
2	30	3.45	0.00118
3	45	4.80	0.00110
4	60	6.15	0.00107
5	75	7.50	0.00105
6	90	8.85	0.00104
7	105	10.20	0.00103
		Average C_1,	0.00112

If now we compare the velocity constants, C, for the first interval of the several series and the average velocity constants C_1 for the several series we obtain the following :

Velocity Constants for the First Interval.

		C.
Series 1		0.00543
" 2	0.00283 × 2	0.00566
" 3		0.00635
" 4	0.00135 × 5	0.00675

Average Velocity Constants.

		C_1.
Series 1		0.00507
" 2	0.00252 × 2	0.00504
" 3		0.00575
" 4	0.00112 × 5	0.00560

We see, therefore, that the general trend of these results indicates that the amount of the ethyl butyrate hydrolyzed by lipase is, within certain limits, independent of the concentration of the ethereal salt, thereby confirming our earlier results on this phase of the problem. The fact that the rate of hydrolysis is slightly higher the more dilute the solution of ethyl butyrate, and that somewhat larger amounts of the ester are hydrolyzed in the more dilute solutions is doubtless to be explained by the fact that in the more concentrated solutions the acid resulting from the hydrolysis reaches a greater con-

centration than in the more dilute solutions, and hence exercises a greater inhibiting action on the ferment.

The Comparative Activity of Lipase, Hydrochloric Acid, and Sodium Hydroxide towards Ethyl Butyrate.

So little is known as to the real nature of the hydrolyzing enzymes, that it seemed to us of interest to compare lipase with dilute hydrochloric acid and caustic soda, as to their power to hydrolyze ethyl butyrate, since all three of these substances can effect the decomposition of ethereal salts. A clear solution of lipase was employed, 5 cc. of which gave, on evaporation and drying in the air at 110° C., 0.0047 gram solid residue. As already pointed out above, it is not at all probable that all of this solid residue consists entirely of the ferment. On the other hand, considering the great variety of substances present in the liver, it seems more than likely that only a small amount of this residue consists of the lipolytic ferment. For the purpose of comparison, however, it was considered advisable to regard it as consisting of pure lipase, and to compare it therefore with about an equal quantity of hydrochloric acid and caustic soda, in estimating their respective hydrolyzing powers.

Accordingly three experiments were arranged as follows:

1. Twenty-five cc. of a clear solution of lipase were neutralized with dilute sodium hydroxide and made up to 50 cc. To this, 25 cc. of ethyl butyrate solution were then added and the mixture allowed to stand at 20° C. for the desired time. At the end of certain intervals 10 cc. of the mixture were withdrawn by means of a pipette and titrated with N/100 sodium hydroxide. The results obtained were as follows:

Time in minutes.	N/100 sodium hydroxide required. cc.	Percentage of ethyl butyrate hydrolyzed.
0	0.0	0.0
85	5.8	6.92
155	8.3	9.90
1218	11.8	14.07

2. Five cc. N/10 sodium hydroxide were mixed with 45 cc. of water and 25 cc. of ethyl butyrate solution. This mixture

was then allowed to stand at 20° C., and at certain intervals 10 cc. of it were withdrawn by means of a pipette and a quantity of hydrochloric acid added equivalent to the amount of caustic soda originally present. The excess of acid, corresponding to the amount of ethyl butyrate saponified in the given time, was then titrated with N/100 sodium hydroxide. The results of these measurements are as follows :

Time in minutes.	N/100 Sodium hydroxide required. cc.	Percentage of ethyl butyrate decomposed.
0	0.0	0.0
86	5.11	5.22
158	5.91	5.33
164	6.06	6.19
1220	6.31	6.44

3. Five cc. N/10 hydrochloric acid were brought together with 45 cc. of water and 25 cc. of ethyl butyrate solution, and allowed to stand at 20° C. for a certain time. At intervals, 10 cc. of the mixture were withdrawn and titrated with N/100 sodium hydroxide. After making allowance for the initial acidity, the following results were obtained :

Time in minutes.	N/100 Sodium hydroxide required. cc.	Percentage of ethyl butyrate hydrolyzed.
0	0.0	0.0
86	0.0	0.0
167	0.0	0.0
1224	0.2	0.204

It is evident from these results that lipase probably far exceeds both caustic soda and hydrochloric acid in its power to hydrolyze ethyl butyrate in dilute solution. It is further evident that it cannot partake of the nature of an acid, since even one of the strongest acids known, namely, hydrochloric, is far removed from it in its power to hydrolyze ethyl butyrate. On the other hand, it would seem reasonable to conclude that if this ferment has any analogue at all among ordinary chemical compounds, it more nearly resembles sodium hydroxide than it does hydrochloric acid, at least, in so far as its action on ethyl butyrate is concerned. In this connection it is interesting to note that Hanriot has reached similar conclusions

respecting the chemical nature of lipase from altogether different premises. According to this observer, the basic nature of lipase would not only explain its power to hydrolyze ethereal salts but would also enable us to understand the inhibiting and destructive action of acids on the activity of the ferment.

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AMMONIUM SULPHOCYANATE AND THIOUREA AS SOURCES OF NITROGEN TO FUNGI AND MICRO-ORGANISMS.

BY JOSEPH H. KASTLE AND ELIAS ELVOVE.[1]

It occurred to one of us, Kastle, that it might prove of interest to determine to what extent the nitrogen of ammonium sulphocyanate and thiourea is available for the life and growth of fungi and micro-organisms, and also to what extent we could discriminate between these isomers by biochemical methods.

In this connection it may be observed in passing that the sulphocyanates and thiourea suffer no change in the animal organism. That such is the case we must conclude from the work of Pollak[2] and from certain unpublished results obtained by Kastle in 1902. The former found that sodium sulphocyanate, when administered by the mouth, and subcutaneously to man and the lower animals, could be practically all recovered from the urine unchanged, and also that the "surviving liver" had no power of decomposing the sulphocyanates. The following experiments were carried out by Kastle: 0.5 gram of ammonium sulphocyanate in a small amount of water was injected subcutaneously into a guinea pig. For some time no effects were observable. In about an hour, however, the animal became restless and convulsions soon set in, which were much intensified by any sudden noise or irritation. The animal died in two and a half hours after the injection, in all probability from ammonium poisoning. The post-mortem examination showed some fatty degeneration of the liver, and

[1] Research Assistant in the Carnegie Institution of Washington.
[2] Beitr. chem. phys. Path., 2, 430–433 (1902).

the intestines were greatly distended with gas. The bladder was empty and no urine was passed during the experiment. The blood and several of the tissues and organs gave abundant tests for sulphocyanate, indicating that this compound is not converted into thiourea in the organism; in fact, there was nothing to indicate that it had been changed in any way.

To a second pig, 0.5 gram of thiourea was administered subcutaneously. At first this pig exhibited greater distress than did the one which received the ammonium sulphocyanate. At the end of an hour, it was observed to be in a somewhat listless, semi-comatose condition. It completely recovered over night, however, and remained healthy and active until the conclusion of the experiment. During the progress of the experiment it passed urine freely. This was collected twenty-four and forty-eight hours after the injection, and on both occasions was found to contain an abundance of thiourea, but no sulphocyanate. From these results, together with those of Pollak, it would seem that both of the compounds remain unaltered in the animal organism.

Such being the case, it occurred to us to study the growth of certain fungi and micro-organisms in nutritive solutions containing these two substances as nitrogenous food material. Accordingly a nutritive solution was prepared, containing 25 grams of cane-sugar, 0.25 gram calcium phosphate, 0.2 gram potassium carbonate, 0.2 gram magnesium carbonate, and 0.2 gram potassium phosphate in 500 cc. of distilled water. To 200 cc. of this solution 0.5 gram of ammonium sulphocyanate was added, and to a second portion of 200 cc. of the original solution 0.5 gram of thiourea was added. These solutions were labeled I. and II. respectively. Six tubes were then prepared containing about 5 cc. each of solution I. and similarly a series of tubes with solution II. These tubes were then sterilized and inoculated with a pure culture of green mold, *Penicillium glaucum*, on November 4th, after which they were put away in a dark closet at room temperature, and examined from time to time for growth of the mold with the following results:

Time.	I.	II.
5 days	Three of the tubes showed vigorous growth of mold. Fructification in one tube.	No distinct growth in any of the tubes.
10 days	Plentiful growth in all tubes. Fructification in one tube.	Very uncertain and sparing growth in one tube.
15 days	Vigorous growth with fructification in all tubes.	Sparing growth of mycelium in two out of six tubes.

It is evident from these results that at least a part of the nitrogen of ammonium sulphocyanate is available or the growth of the green mold, whereas that of thiourea cannot support the growth of this fungus. In order to determine whether the thiourea was really poisonous to the spores of the mold, or whether it simply could not furnish the nitrogen essential to the plant, portions of solution I., containing ammonium sulphocyanate, were inoculated with some of the material that had remained in contact with solution II., containing the thiourea, for fifteen days. After three days, growth had started in all except one of the tubes thus prepared, and after fourteen days there was growth in all of the tubes of this series, indicating that while the thiourea is not poisonous to the fungus, its nitrogen is unavailable for its growth. It further appears that only the ammonium nitrogen of ammonium sulphocyanate is available for the needs of the plant. That such is the case may be gathered from the following experiments with potassium sulphocyanate.

A solution similar to solution I. was prepared, except that it contained 0.5 gram of potassium sulphocyanate instead of ammonium sulphocyanate. Six tubes containing this solution were inoculated with spores of *Penicillium glaucum*. At the end of fourteen days no growth of the mold was to be observed in any of these tubes; 0.05 gram of ammonium tartrate was then added to each tube, after which they were allowed to stand for a further interval. Ten days after the addition of the ammonium tartrate an abundant growth with fructification was observed in four out of the six tubes. It would seem, there-

fore, that while the sulphocyanate ion is not poisonous to the fungus, the nitrogen thereof is not available for its growth.

Similar results have been obtained with yeast. A nutrient solution, A, was prepared, containing the following substances:

Potassium phosphate	1.0 gram
Calcium phosphate	0.1 "
Magnesium sulphate	0.1 "
Cane-sugar	75.0 grams.
Water	500 cc.

To 100 cc. of this solution 0.5 gram of ammonium tartrate was added; to a second portion of 100 cc. of the solution 0.5 gram ammonium sulphocyanate was added, and to a third portion of the solution, 100 cc., there was added 0.5 gram of thiourea. The three solutions were then sterilized and inoculated with a culture of pure yeast, after which they were put in the incubator and kept at 30° C. for several days. At the end of three days, the flasks containing the ammonium tartrate and sulphocyanate showed an abundant growth of yeast, whereas the flask containing the thiourea showed none, or at most a mere trace. The flasks containing the ammonium tartrate and sulphocyanate both developed a strong alcoholic odor, whereas the flask containing the thiourea gave no evidence of alcoholic fermentation.

On the other hand, it is interesting to note in this connection, that while thiourea is unable to supply the nitrogen necessary for the growth and reproduction of the yeast, it does not prevent alcoholic fermentation, provided a sufficient amount of yeast is present originally in the saccharine liquid. That such is the case may be seen from the following experiments:

Three flasks were prepared, each containing 50 cc. of nutritive solution A. To one of these 0.1 gram of ammonium tartrate was added, to the second 0.1 gram of ammonium sulphocyanate, and to the third 0.1 gram of thiourea. 0.1 gram of yeast was then added to each flask. On standing over night at 30° C., all three flasks showed alcoholic fermentation. This

experiment was repeated, using glucose instead of cane-sugar, with essentially the same results.

The difference between ammonium sulphocyanate and thiourea, so far as the availability of nitrogen is concerned, has also been demonstrated by means of the various micro-organisms of putrid cheese. A nutrient solution was prepared, containing the following substances:

Calcium phosphate	0.25 gram
Potassium phosphate	0.20 "
Potassium carbonate	0.20 "
Magnesium sulphate	0.20 "
Cane-sugar	25.00 grams
Water	500 cc.

This solution was divided into five equal portions: To (1) nothing was added; to (2) 0.1 gram ammonium chloride; to (3) 0.1 gram potassium nitrate; to (4) 0.1 gram ammonium sulphocyanate; and to (5) 0.1 gram thiourea. These solutions were placed in flasks and sterilized, after which they were inoculated with putrid cheese. The flasks were then placed in the incubator and kept at 30° to 35° C. At the end of one week flasks (2) and (4) showed an abundant growth of micro-organisms, whereas no bacterial growth was observed in the other three. At the end of three weeks the flask containing the ammonium sulphocyanate showed the most abundant growth of any of the flasks, being literally filled with mold and other organisms. The flask containing the ammonium chloride also contained an abundant growth. The flask containing the thiourea showed only very slight growth, as did the flasks containing the potassium nitrate and no other nitrogen compound.

Conduct of Ammonium Sulphocyanate and Thiourea towards the Nitrifying Organisms of the Soil.

In view of the fact that the nitrogen of ammonium sulphocyanate is available to certain fungi and micro-organisms, whereas that of thiourea is not, it occurred to us that these two compounds might conduct themselves differently to the

nitrous and nitric organisms of the soil with respect to the formation of nitrite and nitrate.[1]

With the view, therefore, of testing the conduct of these two isomers towards the nitrifying organisms of the soil the following experiments were carried out:

Four solutions were prepared: No. 1 contained 0.1 gram of ammonium chloride, 0.002 gram of magnesium sulphate, 0.004 gram of potassium phosphate, an excess (0.5 gram) of calcium carbonate, in 100 cc. of water.

No. 2 differed from No. 1 only in that it contained 0.1 gram urea in place of the ammonium chloride.

No. 3. Same as No. 1 except that it contained 0.1 gram ammonium sulphocyanate instead of ammonium chloride.

No. 4. Same as No. 1 except that it contained 0.1 gram thiourea in place of ammonium chloride.

To each of the solutions 0.1 gram of pasture soil was added, and small portions of the several mixtures tested at once for nitrates and nitrites with diphenylamine and Griess' sulphanilic acid reagent. None of the solutions gave the slightest test with either of the reagents. The flasks containing the several mixtures were then closed with a plug of cotton wool and kept in the dark, at room temperature, for a number of days. They were then tested from time to time with diphenylamine with the following results:

	Color with diphenylamine.			
Time.	1.	2.	3.	4.
19 hours	Light blue	None	None	None
41 "	Blue	Light blue	"	"
89 "	Dark blue	" "	Faint blue	"

At the end of fifteen days the quantity of nitrite in each of the solutions was determined colorimetrically with the sulphanilic acid reagent, with the following results:

Solution.	Milligrams N_2O_3.
1	1.2
2	0.40
3	0.03
4	None

[1] Since this communication was written we have come across an observation by Munro, bearing on this subject. This observer found that the thiocyanates are easily nitrified by soil, whereas thiourea resisted nitrification for three years. J. Chem. Soc. (London), Trans., 49, 638 (1886).

After twenty-three days the following numbers for N_2O_3 were obtained:

Solution.	Milligrams N_2O_3.
1	10.0
2	8.0
3	0.20
4	None

No. 4 also gave no reaction with diphenylamine. It would seem, therefore, that in the conduct of the nitrifying organisms of the soil towards ammonium sulphocyanate and thiourea, we have an interesting confirmation of the observations of Omeliansky.[1] According to this observer the nitrogen of organic compounds is not directly attacked by the nitrifying organisms, but must first be converted into ammonia. It is known that urea is very readily hydrolyzed by bacteria, yielding ammonium carbonate, a compound which would readily undergo nitrification in the presence of soil organisms. On the other hand, thiourea is hydrolyzed with great difficulty. By the action of hydrolyzing agents it is transformed into its isomer ammonium sulphocyanate, but even this change does not seem to be brought about by water alone or in the organism. Hence we find that while ammonium sulphocyanate is slowly nitrified, thiourea is not acted on by the organisms of the soil, or if so, then only with extreme slowness as compared with ammonium sulphocyanate.

In this connection some observations on the oxidation of ammonium sulphocyanate and thiourea by hydrogen peroxide are not without interest. In the course of some experiments on the oxidation of ammonium salts by hydrogen peroxide, one of us, Elvove, has observed that nitrites are formed from ammonium salts by the action of hydrogen peroxide, provided there is present a third substance which is capable of liberating some free ammonia, such as sodium or calcium carbonate, or an oxygen carrier, such as manganous chloride, and that in the presence of the two classes of substances the amount of nitrite produced is much greater than the sum of the amounts of nitrite produced in the presence of either alone. It there-

[1] Centrbl., 1899, II, 347.

fore occurred to us to test the conduct of ammonium sulphocyanate and thiourea towards hydrogen peroxide in the presence of calcium carbonate alone and in the presence of both calcium carbonate and manganous chloride. Four tubes were prepared as follows:

No. 1 contained 0.2 gram calcium carbonate, 0.1 gram ammonium sulphocyanate, and 5 cc. of a one per cent. solution of hydrogen peroxide.

No. 2 was same as No. 1, except that it contained in addition 0.1 gram manganous chloride.

No. 3 was same as No. 1, except that it contained 0.1 gram thiourea, instead of the ammonium sulphocyanate of No. 1.

No. 4 was same as No. 3, except that it contained, in addition, 0.1 gram manganous chloride.

After standing at ordinary temperature for fifteen hours, the following results were obtained:

No. of experiment.	Milligrams N_2O_3.
1	0.03
2	0.10
3	None
4	"

It is thus seen that in the case of thiourea no nitrite is produced, even in the presence of both calcium carbonate and manganous chloride, whereas ammonium sulphocyanate under the same conditions produces quite a measurable quantity of nitrite. That these isomers behave differently towards hydrogen peroxide just as they behave differently as sources of nitrogen for fungi and microrganisms is certainly interesting and significant.

A similar study of other isomeric nitrogen compounds as sources of nitrogen to the growing plant is now being carried on in this laboratory.

STATE COLLEGE OF KENTUCKY,
LEXINGTON, KENTUCKY,
February, 1904.

Contribution from the Chemical Laboratory of Harvard College.

THE SPECIFIC GRAVITIES OF LITHIUM CHLORIDE, BROMIDE, AND IODIDE.

By Gregory Paul Baxter.

Accurate determinations of the specific gravities of salts are very rare.[1] Furthermore, owing to almost entire lack of mention of the methods employed or the data obtained, it is seldom possible to decide how much dependence to place upon a given value. It seems worth while, then, to publish the following determinations of the specific gravities of some common salts, with full particulars concerning the methods of preparing the material and the carrying out of the determinations.

The three halides of lithium were made from lithium carbonate. This salt was obtained in a pure state by first boiling a solution of lithium carbonate in nitric acid with an excess of the carbonate, in order to precipitate all metals except those of the alkalies. Sodium and potassium were then eliminated from the filtered solution by double precipitation of the lithium as carbonate by means of ammonium carbonate. The precipitate was washed with water several times after each precipitation. When examined upon a platinum wire in the Bunsen flame no evidence of sodium was visible to the naked eye, although spectroscopically traces of this metal could be detected. The purified lithium carbonate was converted into the halides by solution in the corresponding halogen acids.

Hydrochloric acid was purified by distillation, with the use of a platinum condenser, the distillate being collected in a platinum dish. Hydrobromic acid, which had been prepared by Mr. J. B. Churchill, was similarly treated. The bromine from which this acid was made had been freed from chlorine by solution in aqueous calcium bromide and subsequent distillation. By means of red phosphorus and water the bromine was converted into hydrobromic acid and the acid was distilled to free it from the excess of bromine and any iodine

[1] See Richards and Rogers: Proc. Amer. Acad., 31, 163; Baxter and Hines: This Journal, 31, 220 (1904); Baxter and Lamb: *Ibid.*, 31, 229 (1904).

which it contained, as well as from phosphoric acid. Finally, one of the middle fractions of the acid was distilled, as stated above, with a platinum condenser.

The preparation of pure hydriodic acid was a somewhat more difficult undertaking. The method ordinarily employed to free iodine from chlorine and bromine, that of sublimation from potassium iodide, is a troublesome process, hence Stas' method of distilling the iodine from aqueous potassic iodide was used. A considerable quantity of iodine was dissolved in a concentrated solution of potassium iodide, and the solution was boiled in a retort, the neck of which delivered into a flask packed in ice. Although at first the iodine condensed on the neck of the retort, no difficulty was experienced through clogging, and eventually the current of steam carried all the iodine into the condensing-flask. With equal ease the iodine was again distilled from pure water. Chlorine and bromine must be removed by this method at least as completely as by the method of sublimation, while the process requires not one-quarter the time ordinarily consumed in subliming the substance. The iodine obtained in this way is hopelessly moist, so that it could not be used for purposes of standardization without sublimation and drying, but since it was next converted into hydriodic acid by means of water and sulphuretted hydrogen, moisture was no disadvantage here. The precipitated sulphur was removed by filtration after the excess of sulphuretted hydrogen had been eliminated by boiling for several hours. During the boiling, any hydrocyanic acid resulting from cyanogen impurities in the iodine, must have been removed,[1] although it is improbable that any considerable amount of iodide of cyanogen could have resisted the potassium iodide treatment. Since the hydriodic acid was found to contain sulphuric acid, a small quantity of recrystallized barium hydroxide was added and the precipitated barium sulphate was filtered out. Finally, in order to free the acid from alkaline metals, it was distilled with a platinum condenser. Partial decomposition of the hydriodic acid, with

[1] Richards and Singer found that hydrochloric acid may be completely freed from hydrocyanic acid by prolonged boiling. This JOURNAL, 27, 205.

liberation of iodine, took place during the distillation, so that a trace of platinum was dissolved from the condenser. The iodine and platinum were easily removed, however, in a way to be described presently.

A similar method may be advantageously used to prepare pure hydrobromic acid. Richards and Wells, working in this laboratory, have found that, if hydrobromic acid has been made by the action of bromine on red phosphorus and water, it is difficult to free the acid from last traces of phosphorus by distillation. But in a specimen of hydrobromic acid, carefully prepared after the fashion above not the least trace of sulphuric acid could be detected when the acid was diluted and treated with a considerable quantity of barium hydroxide.

From these three acids the corresponding salts of lithium were made by dissolving pure lithium carbonate in a slight excess of the acid in a platinum dish. The excess of acid was neutralized with ammonia gas and the solutions were evaporated on a steam-bath. The solid residues resulting from the evaporation of the lithium and ammonium chlorides and bromides were pure white and were used directly for the determinations. The solution of lithium and ammonium iodides was freed from platinum and iodine, in one case by heating the slightly ammoniacal solution with pure metallic iron until colorless, and then filtering the solution. In another similar sample (that used in the last determination), sulphuretted hydrogen was passed into the acid solution before the addition of ammonia, and the solution was filtered. Only a negligible amount of sulphate could have been introduced in this way. During the latter part of the evaporation the solution became yellow from the separation of a small amount of iodine. Consequently the salt was allowed to crystallize from concentrated solution, and the crystals were separated from the mother-liquor as completely as possible.

In order to dry the salts, they were fused in a platinum boat, in a current of electrolytic hydrogen. The purpose of the ammonium compounds, introduced in the preparation of the salts, was to counteract the tendency of lithium halides to become basic when heated in a moist condition. Obviously,

so long as ammonium compounds remained in the salt, the production of basic compounds was impossible. Since all but the last traces of moisture must have been eliminated before the complete volatilization of the ammonium salts, the basicity was thus reduced to a minimum.

The fusing of the salts was conducted in a tube of hard glass connected by a ground joint with a bottling apparatus by means of which the boat could be transferred, after being heated, to a weighing-bottle without exposure to moist air.[1] Heat was applied gently at first, till the greater portion of the water had been expelled, then the temperature was increased until fusion had taken place and the fused salt was limpid and free from bubbles of gas. The tube was then allowed to cool, and the boat was transferred to the weighing-bottle and weighed.

The weighing-bottle was provided with two stoppers. One was of ordinary form and was used in the weighing of the salt; the other, which fitted the neck of the weighing-bottle exceptionally well, was provided with two capillary tubes, by means of which the bottle could be filled with any liquid. After the weighing of the salts, the ordinary stopper was removed, enough toluol to cover the boat and salt was quickly poured into the bottle, and the pycnometer stopper, which had been weighed with enough syrupy phosphoric acid to make the joint tight, was inserted. The pycnometer was placed in a vacuum-desiccator, which was then exhausted and the toluol was allowed to boil gently for a few minutes to expel the air contained in the crevices of the salt. By means of the capillary tubes the bottle was completely filled with toluol, and while the pycnometer was immersed as far as possible in a bath of water at 25°, the toluol was adjusted to a mark etched on one of the capillaries. The weight of the system was then determined. After a second adjustment of toluol, the system was again weighed. In every case the two successive weights agreed within two-tenths of a milligram. The weight of the pycnometer containing the empty boat and filled with toluol was determined

[1] Richards and Parker: Proc. Amer. Acad., 32, 59.

three times, the extreme values of the three determinations varying only three-tenths of a milligram. From the average of these three weights, the weight of the salt and the weight of the system, including the salt and filled with toluol, was calculated the specific gravity of the salt.[1]

In one determination with each halide, the toluol from the pycnometer was evaporated, and in no case did any visible residue remain. Evidently the three salts are insoluble in toluol. The aqueous solutions of the fused salts were faintly alkaline to phenolphthalein. In Determination 7 the solution of over three grams and one-half of the iodide required eight-tenths of a cubic centimeter of N/10 acid for its neutralization, but of course this alkalinity was at a maximum in the case of the iodide. No perceptible yellow coloration was imparted to the Bunsen flame by any of the salts. Traces of sodium could be detected with the spectroscope only. Tests for ammonia with Nessler's reagent yielded negative results in the cases where they were applied. The salts were all transparent when cold, and free from gas bubbles as far as could be determined. Contraction during cooling produced cracks between the platinum and the salt, but these must have been filled with toluol during the exhaustion.

The toluol was dried by means of stick potash and was then distilled. In the following table are given the results of three determinations of its specific gravity, made with an Ostwald pycnometer, at 25°:

	Weight of pycnometer. Grams.	Weight of pycnometer filled with water. Grams.	Weight of pycnometer filled with toluol. Grams.
	10.0868	21.3340	19.8035
	10.0868	21.3344	19.8033
	10.0867	21.3341	19.8034
Aver.,	10.0868	21.3342	19.8034

	Grams.
Weight of water	11.2474
Weight of toluol	9.7166
Density of toluol 25°/4°	0.86152

[1] For details concerning the pycnometer and manipulation, see Baxter and Hines: This JOURNAL, 31, 222 (1904).

In the calculations the following vacuum corrections were applied : LiCl + 0.00044 ; LiBr + 0.00021 ; LiI + 0.00015 ; toluol + 0.00126. The weights were carefully standardized to tenths of a milligram, and the corrections of the thermometer at 0° and 32°.38 were determined.

	Weight of salt in vacuum. Grams.	Weight of displaced toluol in vacuum. Gram.	Density of salt. 25°/4°.
LiCl	1.4063	0.5861	2.067
LiCl	1.7288	0.7201	2.069
		Average,	2.068
LiBr	3.0486	0.7584	3.463
LiBr	3.5161	0.8739	3.466
		Average,	3.464
LiI	3.4328	0.7283	4.061
LiI	2.2155	0.4697	4.064
LiI	3.7247	0.7905	4.059
		Average,	4.061

All of the more probable errors in these determinations, such as those due to sodium or potassium compounds, basicity, or the presence of gas bubbles in the solid, would tend to lower the observed specific gravity. Still it is highly improbable that the combined effect of all the errors could affect the second decimal figure. The specific gravities of the salts examined, at 25° referred to water at 4°, are undoubtedly very closely represented by the following numbers :[1]

Fused LiCl, 2.068 ; fused LiBr, 3.464 ; fused LiI, 4.061.

Correction.

Attention should be called to slight errors which were made in the calculations in two recent papers upon the specific

[1] Previous determinations of the densities of these salts are as follows :

LiCl	1.998	Kremers : Pogg. Ann., 99, 62.
	2.074	Schröder : *Ibid.*, 107, 113.
	1.515	Quincke : *Ibid.*, 138, 141.
LiBr	3.102 at 17°,	Clarke : This JOURNAL, 3, 13, 293.
LiI	3.485 at 23°,	*Ibid.*

gravities of cadmium and zinc salts,[1] by the assumption that the vacuum correction of the pycnometer filled with toluol was always the same whether the salt were contained or not. Obviously this is not the case; for although the volume of the system was always the same, the weight of the system containing the salt was always greater than when it was filled with toluol only, and consequently the vacuum correction was less. When allowance is made for this difference, the specific gravities of the salts in question become: Cadmium chloride, 4.047; cadmium bromide, 5.192; silver bromide, 6.473. The error in the case of zinc chloride is far beyond the limit of accuracy of the experiments.

CAMBRIDGE, MASS., Jan. 6, 1904.

Contribution from the New York Agricultural Experiment Station.

VII.—THE NATURE OF THE PRINCIPAL PHOSPHORUS COMPOUND IN WHEAT BRAN.

BY A. J. PATTEN AND E. B. HART.

INTRODUCTION.

From the work reported in Bulletin No. 238 of this station and from other work done preliminary to an investigation of the metabolism of phosphorus in animals, it was found that in many of our ordinary feeding-stuffs a varying percentage of the organic phosphorus was directly soluble in water and in dilute hydrochloric acid. Data illustrating this point will be found in the following table:

Soluble Phosphorus in Oats, Malt Sprouts, and Wheat Bran.

	Solvent.	Total phosphorus.	Soluble phosphorus.	Percentage of total phosphorus.
		Per cent.	Per cent.	Per ct.
Oats	Water	0.355	0.180	50.0
	Hydrochloric		0.096	27.0
Malt sprouts	Water	0.677	0.548	81.0
	Hydrochloric		0.477	70.0
Wheat bran	Water	1.22	1.056	86.5
	Hydrochloric		0.95	77.8

[1] Baxter and Hines: "The Specific Gravities of Cadmium Chloride and Cadmium Bromide," THIS JOURNAL, 31, 220; Baxter and Lamb: "The Specific Gravity of Zinc Chloride," *Ibid.*, 31, 229.

It will be seen that wheat bran carries a much larger percentage of phosphorus than any of the others and that 86.5 per cent is soluble in water.

It was at first supposed that the soluble phosphorus was in combination as nucleins or salts of nucleic acid, but determinations of the amount of soluble nitrogen showed that only about 33 per cent of the phosphorus could be accounted for in this way.

We were therefore led to the conclusion that by far the greater part of the soluble phosphorus was linked up in some other organic combination, since Hart and Andrews[1] have shown that the amount of soluble inorganic phosphorus is exceedingly small.

Attempt to Isolate the Phosphorus Compound.

Two pounds of wheat bran were extracted with 6 liters of 0.2 per cent hydrochloric acid for several hours with frequent stirring. The extract was strained through cheese-cloth and finally filtered through paper.

The filtrate was treated with a large volume of 95 per cent alcohol which threw down a voluminous, flocculent precipitate. The precipitate was allowed to settle to the bottom, the supernatant liquid siphoned off and the precipitate washed with alcohol several times by decantation. It was then dissolved in a small volume of 0.2 per cent. hydrochloric acid, filtered from an insoluble residue, reprecipitated by alcohol, and washed as before by decantation.

This process was repeated, the precipitate finally brought upon a filter, washed with absolute alcohol and ether, and dried at 110° C. The resulting product, which weighed 7.2 grams, was a white, amorphous powder, readily soluble in water.

Its water solution was acid to litmus and it was precipitated from such solution by solutions of salts of the heavy metals, by the alkali metals and the alkaline earths, also by alcohol and ether.

Chemical analysis showed it to be an organic phosphorus

[1] Bulletin 238, N. Y. Agr. Expt. Station.

compound, coupled with calcium, magnesium, and potassium.

0.5004 gram substance gave 0.0082 gram CaO and 0.1327 gram $Mg_2P_2O_7$ equivalent to 1.13 per cent Ca and 5.80 per cent Mg.

0.512 gram substance gave 0.0834 gram K_2PtCl_6 equivalent to 2.60 per cent K.

0.2174 gram substance gave 0.1280 gram $Mg_2P_2O_7$, equivalent to 16.38 per cent P.

0.2122 gram substance gave 0.1438 gram CO_2 and 0.072 gram H_2O, equal to 18.52 per cent C and 3.83 per cent H.

The substance carried also a small amount of nitrogen (0.37 per cent), but this was considered an impurity and, calculated as a proteid, would lower the carbon and hydrogen to 17.30 per cent and 3.63 per cent respectively.

Composition of Isolated Phosphorus Compound.

	Per cent.
C	17.30
H	3.63
P	16.38
Ca	1.13
Mg	5.80
K	2.60

Similar Compounds Reported by Other Workers.

Palladin,[1] working in Schulze's laboratory, isolated from the seeds of black mustard (*Sinapis nigra*) a highly phosphorized compound in combination with calcium and magnesium.

The seeds freed from fat were extracted with 10 per cent sodium chloride solution, filtered, and the filtrate heated to about 80° C. A precipitate separated, carrying with it all of the proteid. The larger part of the precipitate went into solution again on cooling, leaving the coagulated proteid in suspension, which was separated by filtration. The filtrate was again heated and the resulting coagulum collected on a hot-water funnel.

Schulze and Winterstein[2] continued the investigation started

[1] Beitrage zur Kenntniss pflanzlicher Eiweissstoffe; Ztschr. Biol. Jahrgang, 1894, p. 199.

[2] Ueber einen phosphorhaltigen Bestandtheil der Pflanzensamen; Ztschr. physiol. Chem., 22, 90.

by Palladin and obtained a compound carrying 9.65 per cent carbon, 2.83 per cent hydrogen, and 16.13 per cent phosphorus. They thought the substance might be identical with the chief constituent of the globoids found enclosed in the protein kernel of many plant seeds. Pfeffer,[1] in conjunction with Brandau, found that such globoids consist of a calcium-magnesium salt of an organic body coupled with phosphoric acid. What the nature of this organic combination was they were unable to say.

Winterstein[2] isolated a compound from the seeds of black mustard by extracting with dilute acetic acid. The extract was freed from proteid by boiling and filtering when cold. The filtrate was made slightly alkaline with ammonium hydroxide and boiled, the resulting precipitate collected on a hot-water funnel and washed with hot water until the wash-water reacted neutral. The substance was purified by dissolving in dilute acetic acid and reprecipitating with ammonium hydroxide. On removing the calcium with oxalic acid, a product was obtained carrying 18.44 per cent phosphorus and 7.83 per cent magnesium.

By heating the magnesium salt in a closed tube with concentrated hydrochloric acid for thirty hours, at a temperature of 130°–140°, he obtained inosite as a cleavage-product.

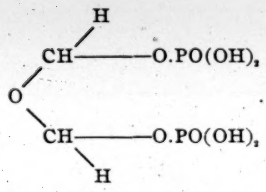
The compound obtained by us from bran by the alcohol method, though still impure, is undoubtedly identical with the one described by these investigators.

Posternak[3] isolated the compound from the seeds of red fir, pumpkin, peas, beans, white and yellow lupine, and also from the potato. He also isolated and identified the free acid as anhydrooxymethylenediphosphoric acid with the following formula :

[1] W. Pfeffer: Untersuchung ueber die Proteinkoerner und die Bedeutung des Asparagins beim Keimen der Samen; Jahrbücher für wissenschaftliche Botanik, 8, 147 (1872).

[2] Ueber einen phosphorhaltigen Pflanzenbestandtheil, welcher by der Spaltung Inosit liefert; Ber. d. chem. Ges., 30, 2299.

[3] Revue Générale de Botanique, 12, 5 and 65, 1900; Compt. rend., 137, No. 3 (20 Juillet, 1903); No. 5 (3 Août 1903) No. 8 (24 Août 1903).



The method adopted by Posternak was the following :

The material was extracted with dilute hydrochloric acid and filtered, the filtrate made alkaline with sodium hydroxide and precipitated with calcium chloride. The calcium chloride precipitate was filtered, washed, and finally dissolved in dilute hydrochloric acid. Sodium acetate was added to the solution to replace the free mineral acid by acetic acid, and copper acetate added in excess. The copper precipitate was filtered, thoroughly washed with water, and decomposed by hydrogen sulphide.

The copper sulphide was removed by filtration and the excess of hydrogen sulphide removed by pumping air through the liquid. It was then evaporated in a vacuum over sulphuric acid.

We found it very difficult to remove the last traces of calcium by this method and have modified it by substituting barium chloride for calcium chloride. This admits of a very thorough washing at this stage of the operation as the barium salt is much more insoluble than the calcium salt, and also admits of a complete removal of the barium as a sulphate.

Method of Preparation of Free Acid.

The method finally adopted by us is as follows :

The bran was extracted with 0.2 per cent hydrochloric acid, strained through cheese-cloth and filtered through paper. Since the compound is present in bran as a calcium-magnesium-potassium salt, it was precipitated directly with copper acetate, by which means we were able to remove the greater part of these bases. After washing the copper precipitate it was suspended in water and decomposed by hydrogen sul-

phide. The filtrate from copper sulphide was made alkaline with sodium hydroxide and precipitated with barium chloride. The barium salt was washed until free from alkali, suspended in water, and dilute sulphuric acid added in sufficient quantity to decompose the salt and throw down the barium as a sulphate. After removal of the barium sulphate by filtration the filtrate was again precipitated in alkaline solution with barium chloride and treated as before. This process was repeated a third time and after final removal of the barium, copper acetate was added in excess. The copper precipitate was filtered at the pump, thoroughly washed with water, and finally suspended in water and decomposed by hydrogen sulphide. The copper sulphide was removed by filtration and the filtrate evaporated on the water-bath to a syrupy consistency.

Analysis of the acid dried at 110° gave the following results:

0.7207 gram substance gave 0.2811 gram CO_2 and 0.2202 gram H_2O equivalent to 10.63 per cent C and 3.38 per cent H.

0.1039 gram substance gave 0.097 gram $Mg_2P_2O_7$ equivalent to 25.98 per cent P.

	Calculated for $C_6H_8P_2O_9$.	Found.
C	10.08	10.63
H	3.36	3.38
P	26.07	25.98

Decomposition of Compound into Inosite and Phosphoric Acid.

Heated with concentrated mineral acids it is broken up quantitatively into inosite and phosphoric acid, according to the following equation:

$$3C_6H_8P_2O_9 + 3H_2O = (CHOH)_6 + 6H_3PO_4.$$

Posternak obtained 97.8 per cent of the total carbon of the acid decomposed as inosite. In our investigation an unweighed portion of the acid was heated in a closed tube with 50 cc. of 30 per cent sulphuric acid at a temperature of 155° to 160° for five hours. After cooling, the tube was opened and the contents washed into a beaker. The sulphuric and phosphoric acids were removed by barium hydroxide and the excess of barium by carbon dioxide. The filtrate was evapo-

rated nearly to dryness, taken up with hot water, and filtered from the remaining barium carbonate. The filtrate was then treated with absolute alcohol and ether until a cloudiness was produced, when it was allowed to stand in the cold. A crystalline precipitate soon separated which was obtained pure after once recrystallizing. It gave the reactions of Scherer and Gallois and melted at 218° to 219° (uncorr.). Inosite melts at 218° (uncorr.).

Carbon and hydrogen determinations were made on the substance dried at 110°.

	Calculated for $C_6H_{12}O_6$.	Found.
C	40.00	39.59
H	6.66	6.78

Properties of Anhydrooxymethylenediphosphoric Acid.

The free acid dried slowly over sulphuric acid is a very thick, transparent liquid, of a yellowish-brown color. It is soluble in all proportions in water and alcohol; insoluble in ether, benzene, chloroform, and glacial acetic acid. It has a very sharp acid taste. Heated to 110° it becomes decidedly brown without decomposition. The alkali salts of the acid are freely soluble in water. Water solutions of the free acid are precipitated by ferric chloride, the precipitate being soluble in an excess of the reagent. Silver nitrate precipitates solutions of the free acid only after a liberal excess of the reagent has been added. The precipitate is insoluble in excess of the reagent. The free acid is not precipitated by the chlorides of magnesium, calcium, barium, or strontium, on account of the liberation of free hydrochloric acid. However, when solutions of the alkaline salts of the free acid are treated with the above reagents a precipitate is formed.

The magnesium and calcium salts are somewhat soluble in water, the barium and strontium salts very sparingly soluble. The magnesium salt is easily soluble in acetic acid, the calcium salt less so, while the barium and strontium salts are very insoluble. All are readily soluble in mineral acids.

The free acid is tetrabasic and forms two salts, the one a normal salt, the other an acid salt. The normal salt reacts

neutral to phenolphthalein, while the acid salt reacts neutral to methyl orange, which may be shown by the following determinations: Ten cc. of a solution containing 0.0648 gram of the acid titrated to phenolphthalein with decinormal barium hydroxide required 10.9 cc. or 0.0748 gram barium. 0.0648 gram of the acid should require 0.0749 gram barium to produce the normal salt, $C_3H_4P_2O_9Ba_2$. Ten cc. of the same solution titrated to methyl orange with decinormal barium hydroxide required 5.1 cc. or 0.035 gram barium. 0.0648 gram of the acid should require 0.0343 gram barium to produce the acid salt, $C_3H_6P_2O_9Ba$.

Quantitative Estimation of the Acid in Wheat Bran.

We extracted 10 grams of bran to 500 cc. with 0.2 per cent hydrochloric acid, made 100 cc. alkaline with sodium hydroxide, precipitated with barium chloride, filtered, and washed free from alkali.

The phosphorus was determined directly in this precipitate.

Total phosphorus. Per cent.	Phosphorus in barium precipitate. Per cent.	Percentage of phosphorus in barium precipitate to total phosphorus. Per cent.
1.35	0.92	68.1

Practically all of the phosphorus soluble in 0.2 per cent hydrochloric acid is in this form, as shown below:

Total soluble phosphorus. Per cent.	Phosphorus in barium precipitate. Per cent.	Percentage of phosphorus in barium precipitate to total soluble phosphorus. Per cent.
0.94	0.92	97.9

Summary.

1. Practically all of the soluble phosphorus of wheat bran is of an organic nature.

2. The organic compound exists in the bran itself as a magnesium-calcium-potassium salt of a phospho-organic acid.

3. The free acid corresponds to the formula $C_3H_8P_2O_9$, and is probably identical with Posternak's anhydrooxymethylenediphosphoric acid.

4. The alkali salts of this acid are freely soluble in water.

The calcium and copper salts are slightly soluble, while the barium and strontium salts are but sparingly so.

5. The acid and its salts seem to be of wide distribution in the vegetable kingdom, having already been isolated from the seeds of red fir, peas, beans, pumpkin, red and yellow lupine, also from the potato and other tubers and bulbs.

In conclusion we wish to say that this forms part of the research on the metabolism of phosphorus and sulphur in the animal body conducted under the direction of Dr. Jordan. The physiological rôle of the acid and its salts in animal metabolism will be made the subject of future researches.

A NEW REDUCING-AGENT FOR THE PREPARATION OF THIOPHENOL.

By W. P. Winter.[1]

In the summer of 1903 the writer was engaged in preparing in the Chemical Laboratory of the Johns Hopkins University a considerable quantity of thiophenol for use in investigations now in progress. The main features of the method of Otto,[2] proposed in 1877, were followed. Benzenesulphone chloride is allowed to flow slowly into a small flask containing zinc dust and hot water. The zinc salt of benzenesulphinic acid which is thus formed is transferred to a large flask, and the reduction to phenyl disulphide effected at low temperature by nascent hydrogen. Better yields are obtained by allowing the mass at this stage to stand twelve hours or more with excess of granulated zinc or zinc dust. The flask is then heated for several hours on the water-bath with an excess of zinc whereby zinc thiophenolate is formed. Upon acidifying with a large excess of acid and distillation with steam, thiophenol passes over. Notwithstanding the great consumption of time and material, this method is quite superior to others that have been proposed. An outline of the best known methods is here given in historical sequence.

Voigt,[3] in 1861, published a method of reducing benzene-

[1] The writer is under deep obligation to Dr. J. C. W. Frazer for valuable suggestions and assistance in the work described in this paper.

[2] Ber. d. chem. Ges., 10, 3055.

[3] Ann. Chem. (Liebig), 119, 144.

sulphone chloride with nascent hydrogen. He was endeavoring to obtain benzenesulphinic acid. The sulphone chloride was allowed to drop directly on the zinc and acid mixture. One great disadvantage was that a firmly adhering mass was formed which prevented rapid evolution of hydrogen. After allowing the mass to stand twenty-four hours he distilled it and found in the receiver an oily product which he named "benzyl mercaptan," while phenyl disulphide remained in the flask.

Otto says the yield of thiophenol was very moderate, and Stenhouse ascribed the fearful odor mentioned by Voigt to traces of phosphorus compounds formed in the preparation of the sulphone chloride.

Voigt stated that the boiling-point was near 165°, and he correctly described the properties of the substance, *viz.*, insoluble in water, soluble in ether, alcohol, benzene, and carbon bisulphide. It burns with a white flame; produces blisters, difficult to heal, on the skin; the vapor attacks the eyes, while prolonged exposure to it produces dizziness. It forms a number of salts with the heavy metals, and dissolves sulphur and iodine. Heated with strong nitric acid it combines, somewhat violently, to form phenyl disulphide.

Otto,[1] in 1867, attempted to reduce sulphophenylethylene, $C_6H_4SO_2C_2H_4$, with nascent hydrogen, thinking he would obtain a mixed sulphide, $C_6H_5SC_2H_5$, but he obtained instead thiophenol and ethyl alcohol. His method was similar to Voigt's. He described the boiling-point as between 170° and 175°.

Kekulé and Szuch,[2] in 1867, showed that if phenol and phosphorus pentasulphide are heated in certain proportions the principal product is thiophenol. Five hundred grams of phenol yield 30 grams of thiophenol, or about 6 per cent of the phenol used. An increase of the pentasulphide beyond the proportion of 10 molecules of phenol to 1 of the pentasulphide diminishes the yield. Moreover, it is quite impossible to separate traces of phenol from the product. They gave the boiling-point as 167° or 168°.

[1] Ann. Chem. (Liebig), **143**, 205.
[2] Ztschr. Chem., **193**, 300 (1867).

Stenhouse,[1] in 1869, distilled sodium benzenesulphonate in iron retorts. He obtained "phenyl mercaptan," C_6H_5SH, in the portion of the distillate coming over between 165° and 180°, and after redistilling from glass the product attained the constant boiling-point of 172°.5. Phenyl disulphide comes over above 180°, and he observed that this could be reduced to thiophenol by zinc and acid, or, better, by digestion with amorphous phosphorus and hydriodic acid.

Stadler,[2] in 1884, distilled sodium benzenesulphonate slowly in a vacuum with a little more than the equivalent amount of potassium hydrosulphide. Out of 10 grams of the material he obtained a yield of 2.5 grams of thiophenol, while the theoretical amount is 6 grams. Attempts to use larger quantities at one time gave smaller yields. The author commends the method for its rapidity and simplicity rather than for the yield it affords.

In 1886, Otto and Rossing[3] found that on warming phenyl disulphide with potassium sulphide in alcoholic solution there was an almost immediate formation of potassium phenylmercaptide. On treating this with hydrochloric acid and distilling with steam, they obtained free thiophenol. Potassium disulphide, K_2S_2, has no action on phenyl disulphide.

Friedel and Crafts,[4] in 1888, showed that if benzene and powdered sulphur are heated in the presence of aluminium chloride to 75° or 80° until the evolution of hydrochloric acid and hydrogen sulphide ceases, and the mixture is then poured into water, an oily supernatant layer separates which by fractional distillation is separable into three portions: the first, phenyl mercaptan (boiling-point 170° to 173°); the second, phenyl disulphide (boiling-point 288°); the third, diphenylene disulphide (boiling at 364°).

In 1890, Leuckart[5] based a method on the use of phenyl ethyl dithiocarbonate, formed by the interaction of diazobenzene chloride and potassium ethyl dithiocarbonate. This was boiled with alcoholic potash until the solution remained clear

[1] Ann. Chem. (Liebig), 149, 247.
[2] Ber. d. chem. Ges., 17, 2080.
[3] *Ibid.*, 19, 3129.
[4] Ann. chim. phys. [6], 14, 437.
[5] J. prakt. Chem., [2], 41, 187.

on addition of water. The alcohol was removed by distillation, water was added to dissolve the residue, and also zinc dust and acid to prevent oxidation. When steam was passed through, thiophenol came over. The yield was 70 per cent of the theoretical, 7 grams of thiophenol being obtained from 20 grams of ester. The author states that large quantities can be prepared at one time as it is not necessary to purify the ester.

Turning now to the practical laboratory method for the preparation of thiophenol which is most followed, namely, the "Otto method" already mentioned, the chief difficulties encountered were that the low yield and the time involved in carrying through one portion make the production of any considerable amount tedious. The yield seems to be affected by minor details to an unusual degree. Theory requires nearly 30 grams for each 45 grams of benzenesulphone chloride instead of the 18 to 22 grams usually obtained.

Without detailing the many variations of this stock method which were employed in the hope of improving the process, it is sufficient to state that no manipulation of the details of the process by several workers in this laboratory, who have had occasion to prepare large amounts of thiophenol, has succeeded in bringing about the desired yield.

It was at this stage that the suggestion was made to try other reducing agents, and the work was carried on nearly simultaneously with several such agents until a modification of the original method was devised which gave better results.

An account of the reducing agents which proved unsatisfactory is first given in the belief that by some, at least, negative results are valued for the light they throw on the purely scientific as contrasted with the technical side of the subject. It was found that the first step of the reaction could not be advantageously changed. When either iron filings, granulated tin, or tin in a finely divided state was employed to combine with the benzenesulphone chloride, the yield was always inferior to that by the old process. Hence the first step was the formation of zinc benzenesulphinate in the usual way. Iron turnings were tried in the second stage, namely, the re-

duction of the zinc sulphinate to phenyl disulphide, but with indifferent results. Ordinary granulated tin at this point produced a somewhat better yield but still inferior to that of zinc dust. Finely divided tin produced by the action of zinc upon a solution of stannous chloride was more promising, producing, in some cases, a yield equal to that of the old method.

Stannous chloride was then used in the same manner and amount as zinc dust by the Otto method with satisfactory results. It was found that the subsequent heating on the water-bath could be shortened to about one-half hour, and that the use of a small quantity of zinc dust (about 60 grams) at this stage exerted a beneficial action.

While the intermediate products of the reaction were not examined, the behavior of the material in the flask seemed to show that, in all probability, there is more direct reduction to the end product, little phenyl disulphide being formed. The difficulty of the complete reduction of the salts of phenyl disulphide seems to stand in the way of the theoretical yield by the old process. But that a little phenyl disulphide is formed, even when stannous chloride is used, is shown by the fact that the addition of a small amount of zinc dust at the latter part of the second stage of the process results in an increased yield (see appended table).

When the flask has cooled, a moderate excess of hydrochloric acid is added and the mixture is distilled with steam. Practically all the thiophenol comes over in the first 100 or 200 cc.

As the tin is thrown out of the solution in the spongy condition by the addition of zinc dust, it is practicable when working on the large scale to reconvert it into stannous chloride for subsequent use. The yield of thiophenol obtained was practically theoretical.

The following table shows the comparative yields of crude thiophenol obtained for each 45 grams of benzenesulphone chloride:

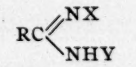
	Thiophenol in grams.
Otto process (zinc dust)	19.5
" " " "	22.0
" " " "	22.5
" " " "	22.5
" " " "	20.0
" " " "	20.0
" " " "	22.0
" " " "	20.0
" " " "	20.0
Fe as reducing agent	10.0
Granulated Sn "	13.5
" " "	19.5
Finely divided Sn	18.0
" " "	19.5
" " "	20.0
$SnCl_2$ without zinc dust	25.5
" " " "	22.5
" " " "	20.0
" " " "	23.5
" " " "	24.5
$SnCl_2$ with zinc dust	28.5
" " " "	30.5
" " " "	30.5
" " " "	27.5
" " " "	26.0

Contributions from the Sheffield Laboratory of Yale University.

CXVII.—ON ISOMERISM IN THE AMIDINE SERIES: DIPHENYLBENZENYLAMINOAMIDINE AND PHENYLBENZENYLPHENYLAMINO-AMIDINE.

By Henry L. Wheeler and Treat B. Johnson.

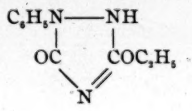
Of the large number of chemists that have had occasion to deal with amidines probably no one has more carefully or more thoroughly investigated the question of their isomerism than von Pechmann. Among his last words on this subject[1] may be found the statement "dass die bekannten Methoden zur Darstellung der beiden stellungsisomeren Amidine,



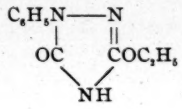
[1] Ber. d. chem. Ges., 30, 1779 (1895).

immer zu einem einzigen Product führen, obwohl Bildungsweisen und Formeln je zwei verschiedenen Verbindungen erwarten lassen.''

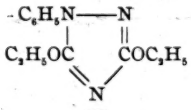
This statement is just as true to-day as it was nine years ago when the above was written. When, therefore, Acree[1] described his so-called 1-phenyl-2-hydro-3-ethoxyurazole, insoluble in alkalies, Formula I., and called attention to the fact that the isomeric compound, II., soluble in alkalies had been made by Wheeler, we concluded that Acree was mistaken in regard to his compound. This result of Acree's being important, if true, we, therefore, prepared the compound, insoluble in alkali, precisely according to his directions and found, as we suspected, that it was not a monoethoxy but a diethoxy derivative,[2] Formula III.



I.



II.



III.

This, therefore, was no exception to the usual experience that such formulas as I. and II. represent a single chemical individual. In a recent note[3] on some of the reactions in the urazole series Acree discusses this point and makes a number of misleading and incorrect statements, not only in regard to our work,[4] but also in connection with the theoretical side of

[1] This JOURNAL, **27**, 120 (1902).

[2] We take this occasion to thank Professor M. M. Richter for calling our attention to the fact that the compound described by Acree (*loc. cit.*) as a dicarbethoxysemicarbazide, and which we showed was a monocarbethoxy derivative, had already been described by Rupe. Ber. d. chem. Ges., **32**, 12 (1899).

[3] This JOURNAL, **31**, 185 (1904).

[4] Being convinced of the accuracy of our results as published in our paper on the molecular rearrangement of amido acid anhydrides (This JOURNAL, **30**, 24 (1903)), and having obtained the data we were looking for, we see no occasion either to repeat our work, as suggested by Acree, or to further discuss the results there described.

the subject. For example, he states: "The possibility of this kind of isomerism is proved beyond question by the isolation of just such tautomeric benzenyldiphenylhydrazidines and the tautomeric methenylphenyltolylamidines."

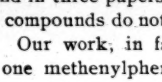
Now, let us examine the references he quotes and certain facts in connection with them. They point in a most emphatic manner to a precisely opposite conclusion.

The first is, curiously enough, to von Pechmann's work in which no case of isomeric benzenyldiphenylhydrazidines occurs whatever, but in the summary of this article von Pechmann states that compounds of the type I. and II. have identical physical and chemical properties, and that they exist in fact in only one form,[1] etc.

Another reference is to Walther's[2] four supposed isomeric methenylphenyltolylamidines, which we have thoroughly examined, and in three papers from this laboratory[3] we showed that these compounds do not exist but are, without exception, mixtures. Our work, in fact, has proved beyond question that only one methenylphenyl-*p*-tolylamidine exists at present. This fact has been recognized by von Pechmann and others.

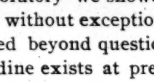
The remaining reference[4] deals with the only case in which von Pechmann observed the formation of isomers when an imide chloride was treated with a base. This unexplained result of von Pechmann's is the only point that deserves further attention in Acree's note.

Von Pechmann states that by the action of phenylhydrazine on benzanilideimide chloride two isomeric amidines were obtained which he provisionally represented as follows:



IV.

m. p. 174°.



V.

m. p. 119°.

[1] Ber. d. chem. Ges., **28**, 869.

[2] J. prakt. Chem., **55**, 41 (1897).

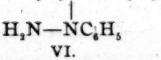
[3] This JOURNAL, **19**, 367 (1897); *Ibid.*, **20**, 853 (1898); Ber. d. chem. Ges., **32**, 35 (1899).

[4] Ber. d. chem. Ges., **28**, 2362.

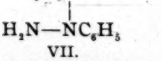
In the very next paragraph he cites arguments to show that these amidines are not to be represented as above, and ends by saying that it must be left undecided in what manner these isomeric amidines are to be represented. He states that tautomerism is excluded here. The above, nevertheless, illustrates how, according to Acree, "the possibility of this kind of tautomerism is proved beyond question."

Of course we do not maintain that such cases of tautomerism or rather desmotropism are impossible but, in view of the careful work of von Pechmann and others all assumed isomers of this sort should be viewed with suspicion and deserve examination.

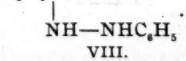
An examination of the properties of the above isomeric amidines of von Pechmann showed that the substances differed decidedly in properties. It suggested to us that the isomerism was due to decided structural differences. It was noteworthy that when benzphenylhydrazideimide chloride was treated with aniline only the high-melting compound was obtained. This, therefore, must have the benzenyl group attached as shown in Formula IV. or V. That isomers resulted in the other case was believed to be due to the fact that phenylhydrazine offers two points of attack to benzanilideimide chloride, as it has frequently been observed to do in the case of other reactive substances,[1] so that in addition to the above, the following compound, VI., would result:



VI.



VII.

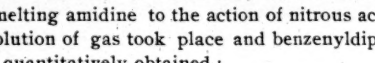


VIII.

A comparison of the properties of these amidines with those of the corresponding benzoylphenylhydrazines then showed a striking similarity. Unsymmetrical benzoylphenylhydrazine, VII., melts lower than the symmetrical and is not affected by mercuric oxide; the low-melting amidine behaves in like manner. The low-melting compounds in both cases are most basic. The high-melting amidine and symmetrical benzoylphenylhydrazine are both oxidized by mercuric oxide, etc.

[1] Busch: Ber. d. chem. Ges., **34**, 322 (1901); *Ibid.*, **36**, 3877 (1903); Frerichs and Beckurts: Arch. Pharm., **237**, 346 (1899).

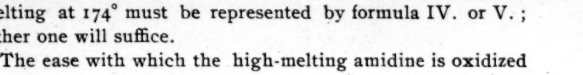
Busch and Holzmann[1] have shown that the corresponding unsymmetrical diphenylthiosemicarbazide gives thiocarbanilide with nitrous acid just as Michaelis and Schmidt[2] have shown that unsymmetrical benzoylphenylhydrazine gives benzanilide under similar treatment; we therefore submitted the low-melting amidine to the action of nitrous acid, whereupon evolution of gas took place and benzenyldiphenylamidine was quantitatively obtained:



VI.

This proves beyond question that the lower-melting amidine has the structure represented by formula VI., and since tautomerism is excluded in this case the isomeric amidine melting at 174° must be represented by formula IV. or V.; either one will suffice.

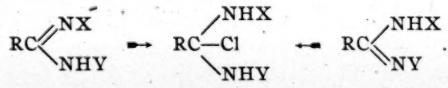
The ease with which the high-melting amidine is oxidized by mercuric oxide is in better accord with formula IV. The oxidation, however, may involve a "1,4-Abspaltung" of hydrogen from structure V., similar to that observed by Thiele[3] in the removal of bromine from other unsaturated compounds. We have found that this amidine reacts immediately and quantitatively with phosgene, giving 1,3,4-triphenyl-1,2,4-triazolone, identical with the substance recently obtained by Busch and Walter[4] by oxidizing benzaldehyde-2,4-diphenylsemicarbazone. This result is most simply explained by considering the structure to be represented by formula V., the reaction being as follows:



To be sure we can assign formula IV. to the amidine, then in this reaction the phosgene must react by addition to the tertiary nitrogen atom.

[1] Ber. d. chem. Ges., **34**, 323 (1901).
[2] Ann. Chem. (Liebig), **252**, 317 (1889).
[3] *Ibid.*, **306**, 108.
[4] Ber. d. chem. Ges., **36**, 1360 (1903).

At any rate the reactions with nitrous acid and phosgene, alone, are sufficient to show that the amidines are structurally different and are not tautomeric or desmotropic forms. In accordance with the fact that the substances are not tautomeric they give different products with various reagents, nitrous acid, phenyl mustard oil, etc. Moreover, if the substances were tautomeric their hydrogen chloride salts would be identical.[1]



The work of von Pechmann has shown, however, that his salts differ widely in properties and therefore are not identical. With these results it is evident that desmotropism in the amidine series remains yet to be discovered.

EXPERIMENTAL PART.

Diphenylbenzenylaminoamidine, $C_6H_5C{=}NC_6H_5$ / $H_2N{-}NC_6H_5$ *and Nitrous Acid.*—Fifty grams of benzanilide and 54 grams of phosphorus pentachloride gave about 42 grams of benzanilideimide chloride boiling at 187°–190° at 19–20 mm. pressure. This was immediately dissolved in ligroin and 53 grams of phenylhydrazine were added; the reaction took place quietly and a cream-colored mass of material separated. The material was dried and extracted three times with hot water. The aqueous extract, on treating with ammonia, gave 10 grams of the crude, lower-melting amidine. It was purified by crystallizing several times from alcohol, whereupon it agreed with the description given by von Pechmann.

Three grams of this material were dissolved in 20 cc. of concentrated hydrochloric acid and 1 gram of potassium nitrite was dissolved in a small amount of water. When these solutions were mixed, a white precipitate separated and gas was evolved. The precipitate proved to be the difficultly soluble hydrochloride of benzenyldiphenylamidine; this was

[1] Stieglitz: This JOURNAL, 21, 109; McCoy: *Ibid.*, 21, 132 (1899).

dissolved in hot water and then ammonia precipitated 2.6 grams of the free amidine, the calculated being 2.8 grams. When crystallized from alcohol the material formed needle-like prisms and melted sharply at 145°.

Some benzenyldiphenylamidine was prepared for comparison from benzanilideimide chloride and aniline. The material thus obtained had all the properties of the above and when portions were mixed the melting-point was not altered.

A nitrogen determination in the case of the material obtained by the action of nitrous acid gave a result agreeing with the calculated for benzenyldiphenylamidine :

	Calculated for $C_{19}H_{16}N_2$.	Found.
N	10.2	10.1

Benzoyldiphenylbenzenylaminoamidine.—A portion of the above aminoamidine was warmed in benzene with the calculated quantity of benzoic anhydride. On evaporating the benzene, washing the residue with ammonia, and then crystallizing from alcohol, colorless, rhombic plates were obtained, which melted at 136°. A nitrogen determination gave :

	Calculated for $C_{26}H_{21}ON_3$.	Found.
N	10.7	10.4

When the higher-melting amidine was treated in the same manner with benzoic anhydride a benzoyl derivative was not obtained.

Phenylbenzenylphenylaminoamidine and Phosgene. — The product which resulted on treating benzanilideimide chloride with phenylhydrazine, after being thoroughly extracted with hot water, was crystallized from a large amount of alcohol, in which it is difficultly soluble. It then agreed in properties with von Pechmann's description of his higher-melting amidine (m. p. 174°–175°).

Three grams of this material were dissolved in chloroform and about 20 cc. of 20 per cent. phosgene in toluene were added ; no precipitate was formed, but on evaporating the solvent on the steam-bath, a residue was obtained which was very difficultly soluble in alcohol, more soluble in benzene,

and still more soluble in chloroform. It formed needles from these solvents and melted at 217°–218°. It had all the properties of *1,3,4-triphenyl-1,2,4-triazolone*, which Busch and Walter[1] have prepared by another method, except that they give its melting-point at 215°–216°. A nitrogen determination gave:

	Calculated for $C_{20}H_{15}ON_3$.	Found.
N	13.41	13.23

The amidine melting at 119° unites with phenyl mustard oil with great energy. The product is a cream-colored powder, very difficultly soluble in benzene and alcohol and it shows no signs of melting at 345°. The isomeric amidine melting at 174° combines with phenyl mustard oil, but with far less energy, and an entirely different substance is formed. It is difficultly soluble in alcohol. When dissolved in chloroform and precipitated with alcohol, needles are obtained which melt at about 186°. The products were not further investigated.

NEW HAVEN, CONN., March 4, 1904.

THE SIGNIFICANCE OF THE MAXIMUM IN THE CONDUCTIVITY CURVES OF KRAUS AT HIGH TEMPERATURES.

BY HARRY C. JONES.

Two papers on the conductivity of solutions of electrolytes at high temperatures have recently appeared. A. A. Noyes and Coolidge[2] have studied the conductivities of two electrolytes in water up to 306°. They found that the conductivities increase very rapidly with rise in temperature, and also that the *dissociation decreases with rise in temperature.* The increase in conductivity with rise in temperature is, of course, due to the increase in the velocities of the ions; but the second point, the decrease in the dissociation with rise in temperature is of special interest in connection with the theory of Dutoit and Aston,[3] connecting the dissociating power of a solvent

[1] *Loc. cit.*

[2] Ztschr. phys. Chem., 46, 323.

[3] Compt. rend., 128, 240 (1897).

with its own association. As the temperature rises, the water becomes less and less associated, as was shown by the work of Ramsay and Shields.[1] As the association of the water becomes less its dissociating power becomes less, and hence the decrease in the dissociation of aqueous solutions with rise in temperature.

Kraus,[2] in his investigation of solutions in methyl and ethyl alcohols, has studied the conductivities up to, through, and beyond the critical temperatures of the solvents. Kraus points out that the conductivity passes through a maximum with rise in temperature. This maximum, in the case of solutions in methyl alcohol, occurs at 150°, while in solutions in ethyl alcohol it is at about 100°. It remains to be seen whether Noyes will find such a maximum in aqueous solutions when he studies the conductivities between 306° and the critical temperature of water. This maximum in the conductivity is of special interest and should be fully interpreted. It is obvious that the conductivity increases with rise in temperature, because the ions move faster at the higher temperature. At the same time the solvent is becoming less and less associated the higher the temperature. As the association of the solvent becomes less, its dissociating power becomes less.

We have then two influences on the conductivity with rise in temperature, and these work counter to each other. The ions move faster and faster with rise in temperature, increasing the conductivity. The association of the solvent becomes less and less with rise in temperature, and, consequently, its dissociating power becomes less and less. This, of course, diminishes the conductivity. The maximum in the conductivity curve represents the temperature at which *these opposite influences become equal.*

These maxima in the conductivity curves are of such importance that their exact significance should be clearly pointed out.

JOHNS HOPKINS UNIV.,
February, 1904.

[1] Ztschr. phys. Chem., **12**, 433 (1893).

[2] Phys. Rev., **18**, 40 (1904).

REVIEWS.

A MANUAL OF QUALITATIVE CHEMICAL ANALYSIS. By J. F. McGREGORY, Professor of Chemistry and Mineralogy in Colgate University. Ginn and Co., 1903.

The methods of separation recommended in this book are good, the directions are clear; it is a very satisfactory manual for a college laboratory. The author does not print the usual tabular schemes for analysis of the different groups, believing that "the use of them in the hands of the majority of students is pernicious." As the great majority of the manuals in use employ the method of tables, its absence will serve as a special recommendation of this book to the many teachers who agree with Professor McGregory on this subject.

E. R.

KALENDER FÜR ELEKTROCHEMIKER, SOWIE TECHNISCHE CHEMIKER UND PHYSIKER, 1904,

It is only necessary to call attention to the appearance of the eighth edition of Dr. Neuberger's electrochemical calendar. This useful little book is now brought up to date, and will be welcomed by all who are interested in electrochemistry.

H. C. J.

DISINFECTION AND THE PRESERVATION OF FOOD. By SAMUEL RIDEAL. New York: John Wiley & Sons. 1903.

This is a reprint of the London edition of this valuable work. The author treats of disinfection first from a mechanical point of view, next sterilization by heat, and third, chemical disinfectants. Under mechanical disinfection he describes the absorption of noxious gases and liquids by charcoal, coke, soot, coal-dust, peat, sawdust, clay, infusorial earth, ashes and cinders, and gypsum. The subject of sand filtration is also fully treated from the sanitary point of view. The effect of low temperature and other dissociation is also included under the mechanical head.

The value of heat as a disinfectant and preserver is treated in Chapter III., in which the principles of heat disinfection are established and the methods of applying it described. The chemical disinfectants are treated under several different heads: First, the halogens and their compounds; second, non-metallic elements and their derivatives; third, metallic salts, organic substances and compounds related to the alcohols.

Chapter XII. deals with practical methods of applying the principles of disinfection and sterilization. It treats of sewers

and drains, sick-rooms, earth-closets, water-closets, infection by flies, furs, wool, and rags. The principles of disinfection of air, water, and its methods of purification and the preservation of timber are described.

Chapter XIII. describes personal and internal disinfection and shows that the common opinion that sachets and lockets containing odoriferous substances are useful is incorrect. The disinfection of cavities of the body is fully described and the necessity therefor accentuated. The utility of antiseptic dressing and of antiseptic hypodermic injections is discussed. Internal disinfection by means of charcoal, chlorinated soda, and sulphides is also mentioned and there is a discussion of the much-mooted question of vaccination. The author calls attention to the fact that modern research seems to indicate that toxines produced by the micro-organisms of infectious disease are the natural disinfectants for combatting it. He states that "Natural immunity is produced either by dissolved alexines or from the resistance of the tissues, whilst acquired immunity is due to the presence of modified bacterial products."

The discussion of disinfection of cuts or abrasions is of general interest since so many serious lesions and often even death are produced by a failure to observe even ordinary precautions when the cuticle is broken. The author states: "If a cut or wound has been accidentally produced, cauterizing with nitrate of silver, nitric acid, phenol, permanganate, or osmic acid is frequently recommended, but the scar left is often very painful and troublesome to heal, besides not being thoroughly safe against inoculation. Covering with lead or court-plaster, or with collodion, painting with iodine, thoroughly drying the cut and painting with a solution of Stockholm tar or Burgundy pitch in alcohol, ether, or acetone, are among the other treatments suggested. None of these give absolute immunity, so that in case of accidental puncture during a post-mortem or operation, or in handling contagious matter such as dead meat, skins, or evacuations, it is probably safest to wash immediately with mercuric chloride, dry, and at once cauterize, and thus combine the two precautionary measures."

If the author means "osmium tetroxide" by the osmic acid mentioned above, its use as a disinfectant should be attended with precautions. Its vapor is very dangerous to the lungs, it acts violently on the skin, causing painful eruptions, and produces intense inflammation of the eyes which often has serious consequences.

The chapter on the sanitary arrangement of dwelling-houses in respect of air, light, heat, wall-paper, furniture, sinks, sick-rooms, and bed-chambers cannot fail to be of great practical help.

That part of the book relative to disinfection extends to page 408 while the part relating to the preservation of food is only 30 pages. This part, whoever, gives a condensed history of the preservation of food by means of salt, niter, aromatic substances, vinegar, etc. The other common methods of preservation are described, such as smoking, salting, preserving in carbon dioxide, and the use of chemical preservatives. Attention is called to the fact that at the International Congress on Hygiene at Brussels in 1903, resolutions were adopted favoring the total abolition of preservatives in all kinds of food. The recommendations of the English Departmental Committee in regard to preservatives are given on page 423. These forbid the use of formaldehyde or formalin absolutely, permit a small quantity of salicylic acid when declared on the label except in the case of milk when no preservative of any kind is to be admitted. In cream, boric acid and borax are permitted when the amount does not exceed 0.25 per cent expressed as boric acid, the amount to be notified by a label. The same preservative is permitted to be used in butter and margarine in proportions not exceeding 0.5 per cent expressed as boric acid. In the case of all foods intended for the use of invalids or infants chemical preservatives of all kinds are prohibited.

The preservation of food by sterilization is fully described, with a brief historical statement.

Whether or not the extreme doctrine of absolute prohibition of all preservatives except those of a condimental nature should be adopted is a matter still open for discussion. Dr. Rideal's book, however, supports the conservative element in this discussion, namely, to the effect that the use of preservatives of a chemical nature, other than condiments, such as sugar, salt, etc., should be discouraged and that in all cases where foods are prepared for invalids and infants they should be prohibited and in all other cases minimum quantities should be used and notification of such use plainly stated upon the labels.

The fifteenth chapter treats of legal statutes and regulations in regard to disinfection. Chapter XVI. deals with methods of analysis which are, necessarily, of the briefest character.

This work will prove of interest both from a scientific point

of view and also in the practical application of the principles of disinfection and food preservation. H. W. W.

LE POINT CRITIQUE DES CORPS PURS. By PROFESSOR E. MATHIAS, of the University of Toulouse. pp. viii + 251. 1904. Paris: C. Naud.

This book contains useful tables of critical data, and useful descriptions of methods of obtaining them. The theoretical part of the book is far less satisfactory, being a forensic in favor of the existence of heterogeneity at the critical point. The argument is, as the author hopes, courteous, but too much emphasis seems to be laid upon the early crude results, and too little upon the recent work of Ramsay (1894), Young (1897), and Villard (1897), in which the importance of an unusual degree of purity is demonstrated. The interesting work of Hagenbach (1901), upon dilute solutions of iodides in sulphurous oxide is discussed at length. These results lead Professor Mathias to admit that the supposed heterogeneity at the critical point is merely temporary—a theoretical improvement upon the earlier attitude regarding it as permanent—but the reviewer thinks that insufficient account is taken of the effect of gravitation in preventing the rapid diffusion of the iodide. This effect alone would cause delay in establishing constancy in composition in the two layers of material. Thus the work of Hagenbach really supports the other argument in favor of a single definite critical volume. T. W. R.

THE ANALYTICAL CHEMISTRY OF URANIUM. By HARRY BREARLEY, joint author of "The Analysis of Steel-Works Materials." Longmans, Green and Co. 1903. 45 pp.

Mr. Brearley has made a special study of the methods of determining uranium, and their availability in the presence of salts of other metals. This book gives the results of the author's work, and is a valuable book for the practical analyst. E. R.

THE ELECTROLYSIS OF WATER; PROCESSES AND APPLICATIONS. By VIKTOR ENGELHARDT, Chief Engineer and Chemist of the Siemens and Halske Co., Limited, Vienna. Translated by J. W. Richards, Lehigh University. Easton, Pa.: Chemical Publishing Co.

As the *raison d'être* for writing this book the author states among other things, in his preface, that "The description given (in the literature) of the form of apparatus is usually only diagrammatic, and often has the object of *deceiving* those who should hope to work in the same direction," and "with the exception of the patent specifications, very little is made public. Every practical electrochemist knows how far the

principles described in the patent specifications are different from the real applications in practice."

It is generally known that technical processes are often kept secret and with the present conceptions that obtain in such matters possibly this is necessary. But that actual *deception* is practiced in such matters must be deplored by every one with ordinary scientific instincts.

Any book which will tend to alleviate this condition of things is most welcome. H. C. J.

TABLES FOR CHEMICAL CALCULATIONS WITH EXPLANATIONS AND ILLUSTRATIVE EXAMPLES. By HORACE L. WELLS, Professor of Analytical Chemistry and Metallurgy in the Sheffield Scientific School of Yale University. 1903. New York: Henry Holt & Company. 58 pp.

This very useful little book is one that might well be on the desk of every analytical chemist. It contains eleven tables, giving a great variety of information. Besides the usual gravimetric factors and their logarithms, atomic weights, weights of gases, barometer corrections, etc., it contains tables of analytical factors involving gas-volumes, metallurgical factors, and a long list of formula (molecular) weights and their logarithms. The table of five-place logarithms is very conveniently arranged with the edges of the pages cut in and indexed as they are in the larger dictionaries. Tables of constants for the boiling- and freezing-point methods, and one for the conversion of English weights and measures into the metric system are appended to the book. Nearly one-half the space is devoted to the explanations, which are clear and made still more so by the well-chosen examples. A few faults were noticed, but they do not detract to any great extent from the value of the book. C. E. W.

ELECTROLYTIC PREPARATIONS. Exercises for Use in the Laboratory by Chemists and Electrochemists. By DR. KARL ELBS, Professor of Organic and Physical Chemistry at the University of Giessen. Translated by R. S. HUTTON, M.Sc., Demonstrator and Lecturer on Electrochemistry, Owens College, Manchester. London: Edward Arnold. 1903. xi + 100 pp.

The German edition of this important aid to the student of electrochemistry has already been noticed in this Journal.[1] It need only be said that the translator has done well in bringing this work within reach of those who are not familiar with the German language. The translation is good and the book is printed in a convenient size for use in the laboratory.

C. E. W.

[1] This JOURNAL, 29, 618 (1903).